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OCCUPATIONAL FACTORS IN PULMONARY DUST DISEASE.[1]

By GORDON C. SMITH, M.B., B.S.,

Industrial Health Unit, School of Public Health and Tropical Medicine, Sydney.

THE Third International Conference of Experts on Pneumonokoniosis, held recently in Sydney under the auspices of the International Labour Organisation (1950), adopted the following definition of pneumonokoniosis: "a diagnosable disease of the lungs produced by the inhalation of dust, the term 'dust' being understood to refer to particulate matter in the solid phase, but excluding living organisms" (the term "diagnosable" indicating the presence of signs or symptoms, but not always loss of function).

The implications and scope of this definition are very wide. Whilst pneumonokoniosis in the etymological sense means "dust in the lung" and therefore is applicable to the pulmonary reactions due to all types of dust (and fumes), in practice it has been associated chiefly with silicosis, asbestosis, and in recent years with the lung disease due to coal dust—diseases in which permanent fibrosis occurs and with characteristic radiographic abnormalities.

Of late it has become evident that acute, semiacute and chronic pulmonary conditions may result from inhalation of a variety of dusts, both organic and inorganic, other than silica, asbestos and coal. Although the nature and severity of the tissue reaction vary according to the type of dust and conditions of exposure, the term pneumonokoniosis can be applied to these conditions.

[1] Read at a meeting of the Section of Public Health, Tuberculosis, Tropical Medicine and Industrial Medicine, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

The Occupational History in Pneumonokoniosis.

Whilst the diagnosis of pulmonary dust disease should never be made without proper consideration of the occupational history, medical history, clinical examination and radiographic findings, the first is of special importance. Unless there has been exposure to dust of a harmful nature there cannot be a pulmonary dust disease, no matter what the medical history or clinical examination might indicate, and no matter how closely the radiographic appearances of the lungs simulate those of pneumonokoniosis.

Thorough and detailed inquiries should be made about any process in which the patient may have been exposed to dust—the nature and conditions of the work, the type of dust and duration of employment at the process. Unless these particulars are obtained accurately, the industrial history may be rendered invalid, with resultant error in diagnosis. Negative evidence as to dust exposure is as important as positive; pneumonokoniosis has been diagnosed in certain individuals with suspicious radiographic signs, evidently on the film appearances alone, for a proper inquiry as to the nature of their work would have revealed no history of industrial dust exposure in these cases.

Properties of Dust in Relation to its Disease-Producing Capacity.

Although all dusts, if inhaled in sufficient quantities, may be regarded as being potentially harmful, some are known to be considerably more injurious than others. Important information concerning the potential capacity of a dusty environment to cause disease of the lungs can be obtained from a study of the following factors: (i) the composition and nature of the dust, (ii) the size of the dust particles, (iii) the intensity of exposure, as determined by (*a*) the atmospheric concentrations of the dust, (*b*) the duration of exposure.

The Composition of Dust.

An analysis for the chemical or mineralogical constituents should be carried out on any dust suspected of causing pneumonokoniosis, and, preferably, the air-borne dust should be examined.

The most injurious component of an industrial dust is crystalline free silica (uncombined silicon dioxide—SiO_2). The pulmonary reactions from amorphous or non-crystalline free silica are less severe, while silicates, that is, silica in a combined form, with the notable exception of asbestos (a hydrated magnesium silicate), are less harmful than free silica.

Most minerals which contain silicates also contain some proportion of free silica; compounds of other elements, such as iron, aluminium, calcium, magnesium and potassium, may also be present. Because of the possible modifying or inhibitory influence of certain substances on the action of free silica, the analysis should be not only for free and combined silica, but also, where indicated, for other likely constituents, especially if these by themselves are capable of producing a lung reaction.

In regard to metallic dust and fume, even though there may be no question of the presence of silica, the concentration and chemical analysis of the atmospheric contaminant should be determined in order that a proper appraisal of the suspected hazard may be made.

In the case of siliceous materials, as a general rule and other conditions being similar, the higher the percentage of free silica in a dust, the greater is its capacity to produce disease. When pulmonary disease is caused by dusts which contain lower percentages of free silica than, say, sandstone or quartz, greater exposures due to higher atmospheric concentrations of dust, or to a longer working period, or both, are necessary. Thus pneumonokoniosis has been found in men engaged in "dragging" bricks from continuous or patent kilns. Tests in New South Wales have shown these men to be exposed to very high concentrations of dust containing about 25% of free silica.

The pulmonary changes in coal miners are out of proportion to what one would expect, having regard only to the free silica content of coal dust, which Smith and Whaite (1950) found averaged 1·8% in the under 10 micron fraction of sixteen samples collected from the coal face of five collieries in New South Wales, but a long period of exposure seems necessary to produce disabling pneumonokoniosis.

Asbestos, which contains no free silica, produces a severe pulmonary disease, but the mode of action of the asbestos fibre differs from that of the silica particle.

The pneumonokoniosis conference agreed that an analysis of material from which dust is derived does not of necessity represent the composition of the dust inhaled in an industrial process. The free silica content of air-borne dust may be similar or may be appreciably increased or decreased, compared with that in the parent material, according to the nature of the material and type of industrial process.

The problems associated with exposure to mixed dusts, for example in foundries, are of interest. Foundry dusts may comprise a mixture of carbon, free silica, silicates, iron oxide and other metal particles, as well as particles from carborundum and other abrasive materials. Iron oxide may play some part in the production of the nodular shadows seen in radiographs and may influence the action of silica in the lungs of certain foundry workers apparently affected with silicosis. One may also question whether any of the nodulation seen in films of grinders with apparent pneumonokoniosis is due to particles from metals or synthetic abrasives.

The physical nature of substances, whether hard and dry or soft and wet, influences their capacity to produce dust. Thus the fact that work is being done in sandstone does not necessarily mean that there will be a serious dust hazard, despite the high free silica content of the rock. If the rock was wet and soft, little or no dust would be formed in breaking it up, whereas if it was of a dry, tightly cemented type, dust high in free silica would be generated, because more energy would be required to rupture it.

The Particle Size of Inhaled Dust.

The pneumonokoniosis conference concluded that in the case of fibrous dusts, such as asbestos and certain vegetable dusts, the larger sizes appear to be more harmful, whereas in many mineral dusts the smaller sizes seem to be the most injurious. In general, whilst particles of mineral dusts (except asbestos) exceeding five microns in size are of minor importance, the lower limit of the size of particles causing pneumonokoniosis has not yet been determined.

Particles of the harmful size range cannot be seen with the naked eye, and it is well to remember that a dangerous concentration of dust of this particle size may be present in the air without being seen. A visible dust cloud may contain fine harmful particles as well as those of larger innocuous size.

The actual number and size distribution of dust particles depend upon the method by which dust is produced and the nature of the parent material from which the dust is derived. Experience in New South Wales, like that of investigations elsewhere, is that at least 70%, and in some cases over 90%, of dust particles generated in industrial processes are up to three microns in size. About 5% of coal dust particles and only about 1% of sandstone particles are over five microns in size. Thus not only is there a relatively small production of the larger particles, but such particles settle out from the atmosphere more rapidly than the smaller sizes. Further, it is known that only a portion of inhaled dust is retained permanently in the lungs, most particles of about five microns and larger being removed by the physiological mechanisms of the nasal and upper respiratory passages.

In a recent review of this subject Hatch (1950) suggests that particles smaller than one micron in size may be the principal contributors to silicosis production. Vorwald (1950) showed in animal experiments that "amorphous" silica of particle size down to 0·005 micron produces profound lung changes, and states that the rate of tissue reaction to dust is inversely proportional to particle size.

On the other hand, in regard to asbestos, it appears that the larger particles are more harmful than the smaller and that in the lungs they act as mechanical rather than as chemical irritants (Gardner, 1938). Wyers (1949) states that dangerous fibres measure about 20 microns.

Dust Exposure.

In general, exposure is measured in terms of concentrations of air-borne dust and the period of time during which the individual is exposed to those concentrations; the higher the average concentration of air-borne dust, and the longer the period of exposure, the greater will be the risk of contracting pulmonary dust disease.

In the case of silicosis and related types of pneumonokoniosis, including asbestosis, the disease is usually of gradual onset and slow development. It does not become evident until after exposure for a period of years, the actual time varying according to the type of dust and industry.

Meiklejohn (1949) states that under present conditions in Great Britain silicosis in a diagnosable stage seldom occurs in under fifteen to twenty years' exposure to the risk, and in regard to coal miners, McVittie (1949) gives a similar period for the development of pneumonokoniosis.

My own observations on a group of 416 New South Wales coal miners showed that the average period of exposure in the men with disabling pneumonokoniosis was thirty-four years, their average age being fifty-four years.

Asbestosis apparently occurs after a shorter exposure. Thus Wyers (1949), who investigated 115 fatal cases of asbestosis, found the average exposure had been 10·4 years.

Under conditions of intermittent exposure it is more difficult to predict the likely effect on the lungs than if the exposure was continuous, but the severity of any dust

hazard is usually lessened in such circumstances. This, however, might not apply with very high intermittent exposures.

In the case of metallic and vegetable dusts, the exposure period necessary to produce a pulmonary disturbance is generally much shorter than with other dusts—sometimes months or weeks, or even less, rather than years. In some instances a single exposure may be sufficient to cause a reaction.

The literature contains reports of the occurrence of "acute" or "rapidly developing silicosis" after short exposures to high concentrations of silica dust, and the following notes about a Sydney case are of interest.

In April, 1942, a man, aged thirty-eight years, died three weeks after he had collapsed at work. The significant details of his industrial history were as follows: From 1917 to 1919 he was engaged in coal mining (Cessnock) for two years. From 1931 to 1937 he was with the Water Board, including fifteen months on rock work. From 1937 to 1940 he was for two years a builder's labourer, excavating in sandstone in the sub-basement of a building. Latterly he had been using a "water pick", but earlier had been using a "dry pick" for six months.

His chest had been examined by X rays in 1937, 1940 (on two occasions, the second being some weeks after he had left the basement excavation work), and again in 1942, 17 days before his death. It was only in the film from the last examination that the radiologist reported evidence of "bilateral nodular fibrosis".

At autopsy, aortitis, congestive cardiac failure, and silicosis of the "rapidly developing" type were found. Microscopically the lungs showed generalized, somewhat immature fibrosis, mainly diffuse, but with some tendency to nodular arrangement.

In October, 1939, the New South Wales Division of Industrial Hygiene had investigated the working conditions in the basement of the building where this patient had been employed. Water jets were fitted to the pneumatic picks and an exhaust ventilation system was installed. Nevertheless concentrations of sandstone dust, ranging from 1150 to 10,000 particles per cubic centimetre (by Owens's dust counter) were obtained. The dust conditions in 1937 were probably worse than in 1939; there is little doubt that this patient contracted silicosis as the result of dust inhalation during the period 1937 to 1940.

Occupations, Dusts et cetera, Associated with a *Pneumonokoniosis* Hazard.

The most important risks are those where exposure to dust containing free silica is likely to occur. Among the commoner processes involved are tunnelling, excavating, mining or quarrying in sandstone or quartz; cutting and surfacing of sandstone or granite; sandblasting, dressing and moulding in foundries, especially machine moulding in iron foundries if siliceous parting powders are used; milling siliceous ores; certain pottery processes; in the brick industry, chiefly "dragging" in patent kilns; manufacture of abrasive soaps and powders; manufacture and handling of refractory materials, and metal mining. In several of these instances, and in a number of others not specially mentioned here, the dusts are of a mixed nature but still contain significant percentages of free silica.

Pneumonokoniosis of coal miners has been discussed in other papers and will not be further considered. In regard to asbestosis, which is of very infrequent occurrence in this country, all the evidence from overseas indicates that it is much more common in workers engaged in the processing and fabrication of asbestos in factories (for example, textile work) than in asbestos miners.

In recent reviews of the literature, Perry (1947), Doig (1949) and Middleton (1950) have described disturbances of the respiratory organs due to mineral dusts other than silica, coal and asbestos, and have discussed the reactions due to vegetable dusts.

I propose briefly to mention the more important of these lung disorders, because, although to my knowledge most of them have not been reported in this country, the industries or processes involved in their causation are carried out here or may be conducted in the future, and so we should be familiar with the possible occupational risks.

Before referring to these, however, I wish to make a few comments about the lung changes which have been observed in basalt workers and biograph operators in New South Wales.

Basalt Work.

Basalt (or "blue metal") is a basic igneous rock, composed essentially of a lime-bearing feldspar with smaller amounts of one or other of the ferro-magnesian minerals and a little iron oxide. Free silica is typically absent but may be present up to 2%. Thus basalt is a silicate, with 40% to 50% of silica in combined form (Whitworth, 1947).

Badham (1927) described a case of fine fibrosis of the lungs in a man, aged sixty-one years, who for twenty-five years had worked in a blue metal quarry and crusher house and was exposed only "to the dust of orthoclase basalt, which contains no free silica". This man died, but an autopsy was not performed.

In recent years I have seen two men, aged forty-nine years and fifty-three years respectively, who, as far as could be ascertained, had been exposed only to basalt dust. The first man had been a crusher attendant for fifteen years at the same quarry as Badham's patient, and the second had worked chiefly on the crusher and screens for thirty-five years at another blue metal quarry. The radiographs of both men showed a well-marked, generalized, fine type of nodulation throughout the lung fields; in the film of the first man, who was totally disabled, there were also large shadows suggesting consolidation.

Biograph Operating.

Two brothers, whom I first saw in 1947, were aged forty-one and forty-six years respectively and had both worked in the projection booth at the same suburban cinema—the elder for ten years and the younger for twenty-three years. There was no history of exposure to dust in other employment. The elder man complained of shortness of breath and loss of weight; his brother, of pains and tightness in the chest. The chest radiographs of both men were similar and showed a generalized fine nodulation throughout both lungs. Films of both men taken in 1949 showed no significant change since 1947.

In 1946 the New South Wales Division of Industrial Hygiene had found that the concentration of dust in the air of the biograph box in the cinema concerned was approximately 6000 particles per cubic centimetre of air by the Owens dust counter; the dust particles were mostly about half a micron or less in size. The ventilation in the box was faulty. A sample of dust obtained from the biograph room in 1946 on analysis gave the following result.

Total SiO_2	6·0%
Rare earth oxides	48·0%
$Al_2O_3 : Fe_2O_3$	17·0%
CaO	6·7%
Loss on ignition	2·0%
Copper	Trace
Fluorides	Present
P_2O_5	Present
SO_3	Present

Following the discovery of the unusual pulmonary condition in the two brothers, seventeen biograph operators from fourteen other theatres were submitted to X ray examination. Their period of employment ranged from seven to thirty-seven years, and some had worked in badly ventilated booths. However, no evidence of a lung reaction resembling pneumonokoniosis was found.

Several authorities have investigated gases, fumes and dusts from carbon arcs and the ventilation of motion picture booths. MacQuiddy and others (1939) showed that some of the high-intensity carbon arc ashes appear to cause mildly proliferative reactions when injected intraperitoneally in the albino rat. They state that it might be deduced that, if inhaled in sufficient quantities over long enough periods of time, these ashes might cause a proliferative type of pneumonokoniosis.

On the limited evidence at present available, and in the absence of autopsy studies, it is not possible to say whether the lung condition present in these basalt workers and biograph operators is due to dust. Further, if dust is

responsible, the question arises whether it has caused fibrosis or is merely present as inert deposits.

It seems reasonable to associate the radiographic abnormalities of the basalt workers with inhalation of dust at their employment, but in the case of the biograph operators, whilst occupational factors cannot be ruled out (indeed, one of these men was compensated for "silicosis"), as they were brothers, and as examinations of other operators gave negative results a non-industrial ætiology has to be considered.

Although these cases are incomplete, I mention them in order to emphasize that with present advances in industrial activity and with increasing knowledge of pneumonokoniosis, we must constantly be watching for lung conditions due to dust, not only from new processes, but also in industries and occupations where previously they have not been suspected.

Talc.

Until comparatively recently asbestos was considered to be the only harmful silicate. Now, however, there is evidence of several investigators that talc, a hydrated magnesium silicate which occurs in flaky and fibrous forms and is used in a number of industries, may cause significant lung changes. McLaughlin, Rogers and Dunham (1948) described a case of pneumonokoniosis confirmed at autopsy in a man, aged fifty-one years, who had worked for thirty-seven years in a rubber tire factory, where he had been exposed to a "fair concentration" of talc dust, and who died primarily from rheumatic endocarditis. There was much fibrosis in the lungs and curious bodies similar to absestosis bodies were also present. These authors conclude that talc pneumonokoniosis and asbestosis are similar diseases, and that pneumonokoniosis is probably caused only by the fibrous varieties of talc.

Graphite.

Doig (1949) and Middleton (1950) refer to recent reports by other authorities in Britain, chiefly Dunner and Gloyne, concerning pulmonary disease in graphite workers.

According to Harding and Oliver (1949), graphite (plumbago), which is a crystalline form of carbon, may be mixed with up to 10% of free silica and with other minerals. They point out that grinding of natural graphite produces the greatest dust risk and can lead to a disabling and fatal pneumonokoniosis, which they describe as resembling, both radiologically and histologically, that of South Wales coal workers.

Other Silicates.

Abnormal reactions in the lungs of animals or man have been described following inhalation of dust from china clay, mica, sillimanite and fuller's earth.

Cement.

Cement is mentioned here because of its very widespread use and of questions which periodically arise as to its possible harmfulness. The raw materials from which cement is made are chiefly limestone, which has not more than about 1% of free silica, and shale, which may contain from 20% to 40% of free silica. The finished product has practically no free silica. Gardner and others (1939) examined 2278 employees from 11 cement-making plants in the United States of America. Only eight persons showed evidence of nodular fibrosis attributable to dust, and in six of these exposure to silica dust in previous employment was presumably responsible. Baetjer (1947) showed that in rats exposure to high concentrations of cement dust did not lower resistance to lobar pneumonia and did not produce any acute or chronic pathological changes in the lung tissue.

Metal Fume Fever.

The well-known example of a minor pulmonary reaction, metal fume fever, due to fume rather than to dust, mostly results from exposure to zinc oxide fumes, for example, in brass foundries, or from welding on galvanized iron. It is said to be caused also by fumes of other metals. When it is due to zinc there is an acute febrile reaction or chill, of short duration, and with no permanent lung damage. If other metallic oxides, such as cadmium or manganese, are involved, a more serious pulmonary condition may ensue.

Cadmium.

Johnstone (1948) states that "cadmium has probably more lethal potentialities than any other of the metals". The inhalation of dust or fumes from cadmium compounds, especially the oxide (for example in welding on cadmium-plated surfaces, from the ignition of cadmium and from the use of cadmium in solder) produces irritant effects, which may be severe, in the respiratory tract, perhaps with pulmonary œdema and death.

Beryllium.

The literature on the pulmonary (and other) lesions affecting workers exposed to beryllium is now extensive, many reports having been published during the past five years. Abstracts of the various papers and articles were recently made in Australia by Taylor (1949). Two principal types of pulmonary lesion have been described: an acute pneumonitis and a chronic diffuse granulomatosis. A number of fatal cases have occurred.

It appears that the acute form which may follow a single exposure to toxic fumes occurs mainly among workers exposed to compounds in the extraction and refining of beryllium from the ore beryl, usually within a few weeks of the first exposure.

The chronic or delayed form, which resembles sarcoidosis, is more persistent. A period of from several weeks or years may elapse from the time of the last exposure to the onset and recognition of the disease. This type usually occurs in persons who have been exposed to dust from fluorescent powders containing zinc beryllium silicate, notably in the fluorescent lamp industry. However, eleven cases of the chronic type were recently reported amongst residents in the vicinity of a beryllium-producing plant. There was no history of occupational exposure (Eisenbud and others, 1949).

Manganese.

Doig (1949) mentions that since 1921 a relationship between manganese and pneumonia has been suspected, following reports from Norway and Germany. In England, Lloyd Davies (1946) found that men exposed to dust of oxides of manganese experienced a high incidence of a condition which he called "manganese pneumonitis". No permanent lung changes were observed. Three years later Lloyd Davies and Harding (1949) reported that pneumonitis has continued to affect manganese workers.

Firket (1950) states that chemical pneumonia which follows inhalation of dusts of manganese, vanadium, osmium and beryllium resembles virus pneumonia both clinically and histologically, and he questions whether the dusts themselves provoke the disease or whether they activate viruses.

Iron Oxide.

Doig and McLaughlin (1936) described a fine nodulation in the lung fields of welders who were apparently in good health. Later, following further clinical and radiographic studies by them and other investigators, it became evident that the pulmonary changes were due to the deposition of iron oxide dust, which is present in welding fume and which is relatively opaque to X rays, and that they were not associated with symptoms, abnormal physical signs, or lessened capacity for work. A similar condition has been reported in other workers than welders exposed to iron oxide.

Enzer and Sander (1938) made an autopsy examination of the lungs of a welder whose chest radiograph showed fine nodulation and who died following an accident; there was no fibrosis in the lung tissue.

According to Doig and McLaughlin (1948), the changes due to iron oxide are not necessarily permanent. In one case described by them the abnormal lung shadows completely disappeared some years after cessation of welding, and in another the shadows became less intense.

Dusts from compounds of barium and tin, which are more radio-opaque than iron, are believed to behave similarly to the latter in the lungs.

Aluminium.

Since Denny, Robson and Irwin (1937) showed that experimental animals exposed to quartz dust *plus* 1% metallic aluminium powder did not develop silicosis, considerable interest has been taken in the question whether aluminium dust damages the lungs, and conflicting reports have been published.

The recent pneumonokoniosis conference decided that there was no conclusive evidence that the inhalation of aluminium in any form prevents the development of silicosis in man, or that aluminium powder is of value as a therapeutic agent in human silicosis or that it is harmful when used for this purpose. There was some evidence that under certain conditions the inhalation of aluminium in industrial processes may be harmful and further there was experimental evidence that in animals the inhalation of aluminium dust aggravates pulmonary tuberculosis.

Synthetic Abrasives.

Shaver and Riddell (1947) described an unusual lung disease, with fibrosis, in some cases fatal, in workers engaged in the manufacture of corundum (aluminium oxide). The process involves treating in special electric furnaces a mixture of bauxite, iron and coke at a temperature of 2000° C. Dense white fumes are given off, which, according to Jephcott (1948), consist mainly of alumina and silica.

Riddell (1948) states that the lung condition appears to be induced by an irritant of a chemical nature, but that the precise agent has not been determined.

These findings are of interest because artificial abrasives (for example, carborundum, that is silicon carbide, and aluminium oxide) have such widespread use in industry. The observations of Smith and Perina (1948) and of Bruusgaard (1948) indicate that dust from synthetic abrasives, when inhaled, may produce nodular shadows in the lungs.

Vegetable Dusts.

A variety of respiratory disturbances, some only of a minor nature, have been attributed to dust from vegetable materials, such as cotton, flax, hay, grain, bagasse and timbers. Three examples may be cited.

Cotton: A condition termed byssinosis (chronic bronchitis and emphysema with a tendency to asthma) has been reported, particularly amongst card-room and blow-room workers, in the cotton-spinning industry in Britain and elsewhere. There are no specific X-ray or autopsy findings. The literature has been well reviewed by Caminita and others (1947).

Bagasse: This is of interest to Australians because of the sugar industry here. Bagasse (or megass) is sugar cane after the sugar has been extracted, and is used in the manufacture of wall boards. Since 1941 cases of respiratory disease (bagassosis) have been reported in workers handling bagasse—in England the persons affected were those engaged on a machine ("shredder") which broke up the bales of bagasse. Hunter and Perry (1946) reviewed the literature fully and described eleven cases (one of the patients subsequently died) of acute bronchiolitis and pneumonia, arising from the inhalation of bagasse dust. They considered the disease was most likely caused by fine vegetable dust; however, its exact ætiology has not yet been determined.

Wheat Dust: Investigations have indicated that exposure to wheat dust may result in asthma (Duke, 1935) and an increased liability to respiratory disease (Smith and others, 1941). The fine hairs of the grain are believed to be responsible, at least in part, for these reactions.

Pulmonary Carcinoma.

Where an occupation, which is associated with an apparently high incidence of lung cancer, has involved dust exposure, it is reasonable to consider carcinoma in a discussion of pulmonary dust disease.

The problem has been reviewed briefly by both Doig (1949) and Perry (1947). They mention the high incidence of lung cancer in the Schneeberg miners in Saxony and in miners in the Joachimstal area in Bohemia. Arsenic and radioactive ores are both considered likely causes in these cases. They also refer to reports by various investigators which indicate that workers in chromate factories, and those exposed to arsenic and asbestos, have a high incidence of pulmonary cancer.

In a personal communication Dr. J. H. Blakemore, of Concord, advises that in a chromate factory in New South Wales, which has been operating since 1944, and which at present employs about 100 persons, all workers engaged in the various stages of production have an X-ray examination of the chest before starting work and at three-monthly intervals thereafter. To date, nothing to suggest pulmonary cancer has been found. In its early years this factory had a number of cases of nasal septal perforation and skin conditions due to chrome, and relatively high concentrations of chromates were found in the atmosphere.

Prevention of Pulmonary Dust Disease.

The measures to be applied in the suppression and control of dust, and for the protection of the workers, are essentially the same, irrespective of the industry and type of dust. Briefly, they include the following:

1. The abolition of processes creating harmful dust. If that is not possible, the total enclosure of such processes in mechanically ventilated structures, or their segregation from other operations in the factory. Isolation can be applied either geographically or by time, that is, by carrying out a dusty process when no other workers are in its vicinity.

2. The use of a harmless material in place of one that is dangerous.

3. The removal of dust at its point of origin by local mechanical exhaust ventilation.

4. The use of water or other wetting agent to prevent dust from certain processes becoming air-borne.

5. Electrostatic precipitation.

6. The provision of adequate general ventilation to dilute contaminated air.

7. Maintenance of a high standard of plant cleanliness and housekeeping.

8. Personal respiratory protection of the worker. Respirators should be worn only when other methods of protection are not practicable or for jobs of short duration. They should be well fitting, comfortable and efficient and should be kept clean.

9. Preemployment and periodical medical examinations, including a radiograph of the chest, of workers exposed to a dust hazard.

If these control methods, or such of them as are applicable to a particular industry or process, are conscientiously applied and maintained, workers would be protected against hazardous exposures to dust.

Summary.

The term pneumonokoniosis is defined and its scope briefly outlined; the need for a complete and accurate occupational history in the diagnosis of pulmonary dust disease is stressed.

The potential capacity of a dust to cause disease is discussed, with special reference to its composition and nature, particle size, and intensity of exposure. In addition to dusts containing high percentages of free silica, others, in which free silica is absent (for example, asbestos and certain metals), are capable of producing severe pulmonary damage. In most dusts (asbestos being an exception) the

harmful particles are those less than about five microns in size. Intensity of exposure, which varies for different dusts, depends on the atmospheric concentrations of dust and the duration of exposure. Brief notes of a case of "rapidly developing" silicosis are given.

The main occupations and dusts associated with a risk of pneumonokoniosis are briefly discussed. In addition to diseases caused by silica, coal and asbestos, reference is made to the radiographic abnormalities of certain basalt workers and biograph operators, and to the pulmonary effects of talc, graphite, cement, zinc, cadmium, beryllium, manganese, iron, aluminium, synthetic abrasives, cotton, bagasse and wheat.

The occurrence of pulmonary carcinoma in workers exposed to chromates, arsenic and asbestos is mentioned.

Measures for the control of dust and protection of workers are stated.

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THE CHANGING FACE OF OBSTETRIC INFECTION.[1]

By ARTHUR M. HILL, M.D., D.G.O. (Melbourne), F.R.C.S.E., F.R.C.O.G.,

Gynæcologist to In-Patients, The Women's Hospital, Melbourne.

THE last fifteen years of the half-century now ending have seen the greatest advances of all time in the prevention and treatment of obstetric infection. This is due predominantly to the introduction and development of modern chemotherapy and antibiotic therapy; but important contributory factors are improved bacteriological knowledge and methods of investigation and a clearer appreciation of the place of maternal resistance in combating infection.

It is proposed to review the major effects of these advances on puerperal morbidity, on the death rate of the main bacterial types of puerperal and abortional infection, and on modern obstetric practice, at the Women's Hospital, Melbourne, over the past ten years. During that period 41,643 women, 80% of whom had attended our own antenatal clinics, were confined; and 18,285 cases of abortion, of which 5175 were diagnosed as "septic", were dealt with. The annual morbidity following the confinements is shown in Figure I.

Sulphonamides were in use in the earliest of these years, although the compounds employed were in general more toxic and less efficient than those now available. In addition, they were not always given in adequate dosage, and their use was largely restricted to the therapy of established infection. However, when it is remembered that less than 10% of all cases of obstetric infection are likely to be of a bacterial type responsive to sulphonamide

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therapy, it is not surprising that a pronounced reduction in puerperal morbidity had to await the introduction of antibiotics. Although penicillin came into use late in 1944, it was only in the last three years that it came to be freely employed, and the figures of the last two years coincide with the establishment of routine combined therapy for all patients either suspected of potential infection or showing one rise of temperature above 100° F. Routine combined therapy consists of the administration

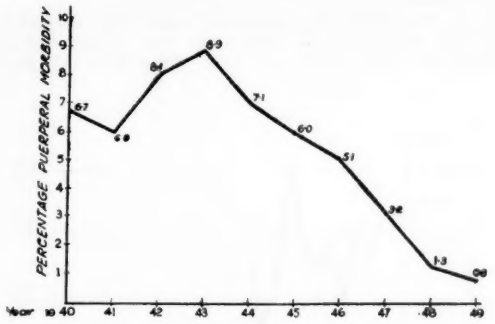

FIGURE I.
Graph showing puerperal morbidity (B.H. standard), 1940 to 1949.

of penicillin, 60,000 Oxford units followed by 30,000 units every three hours, and "Sulphatriad", two grammes followed by one gramme every four hours, both agents to be given for a minimum of five days. These last morbidity figures therefore do not give a true indication of the incidence of puerperal infection, but simply reveal the standard obtainable with a regime designed to minimize morbidity, accelerate wound healing, and shorten the patients' stay in hospital.

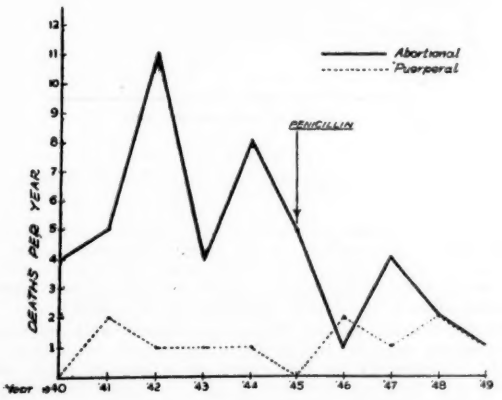

FIGURE II.
Deaths from anaerobic streptococcal infection.

Of considerably greater interest are the features revealed in the methods of management and the outcome of the main bacterial types of puerperal and abortional infection during the last ten years. If experience at the Women's Hospital can be taken as reasonably representative, the problem of obstetric infection in Australia today is largely that of four groups of bacteria: the anaerobic streptococci, *Streptococcus hæmolyticus* group A, *Staphylococcus pyogenes* and *Clostridium welchii*. Less common or less serious types of obstetric infection such as those due to *Bacterium coli*, anaerobic Gram-negative bacilli, hæmolytic streptococci of groups other than A, or fæcal streptococci, will not be considered here. Let us now deal with the four main bacterial types of infection.

Infections with Anaerobic Streptococci.

The anaerobic streptococcal infections are the commonest of all obstetric infections, being responsible for 80% of puerperal and 60% of abortional infections in Melbourne. The source of the bacteria is the genital tract, and spread does not occur from case to case. Although there is considerable variation in bacterial virulence, the invasive ability of the bacteria depends greatly on lowered maternal resistance, in particular on that due to blood loss, and to

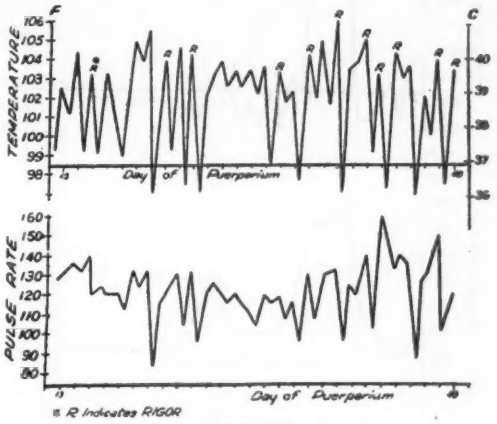

FIGURE III.
Puerperal septicæmia due to anaerobic streptococcal infection, 1941.

a less extent on that due to tissue damage. Immediate smear examination of the vaginal or cervical swab reveals the presence of the bacteria and generally their significance (Butler, 1950).

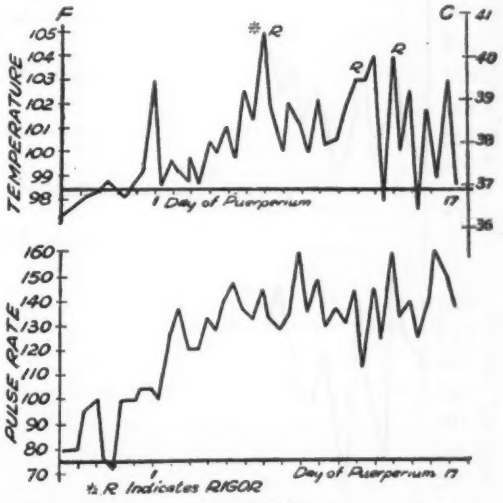

FIGURE IV.
Post-abortional general peritonitis due to anaerobic streptococcal infection, 1942.

Clinically these are the most versatile of obstetric infections, so that although the common picture is nondescript, severe grades may present with any of the following features dominant: "swinging" temperature with rigors, collapse, progressive anæmia, hepatic jaundice, general peritonitis, or renal inhibition.

Control of infection depends primarily on the avoidance of blood loss and tissue damage; next, on the early and

free use of blood transfusions; and finally on the use of penicillin, aided, in thrombophlebitic cases or when infection complicates surgery, by anticoagulants. It needs to be repeatedly emphasized that the commonest early

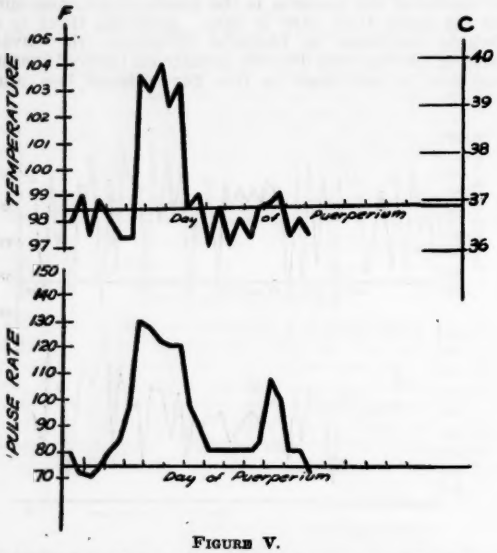

FIGURE V.
Puerperal septicæmia, anaerobic streptococcal infection, 1947.

requirement of these patients is blood, and that its early and generous use will significantly reduce the number and severity of the infections requiring penicillin.

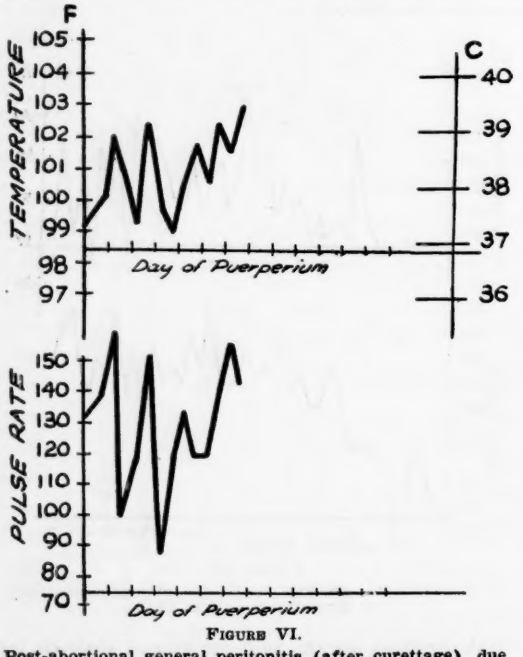

FIGURE VI.
Post-abortional general peritonitis (after curettage), due to hæmolytic streptococcus Group A, 1940.

The mortality from anaerobic streptococcal infections over the last decade is shown in Figure II.

Although the death rate fluctuates considerably, great improvement has followed the introduction of penicillin and the establishment of an efficient blood transfusion service. In the five years preceding the use of penicillin there were 37 deaths, and in the five years following it, 19.

A more significant indication of the value of penicillin than that revealed by mortality statistics is the improved speed and nature of convalescence of patients with these infections who, though gravely ill, do not die. Except in the rare fulminant or resistant case, or when the patient has been admitted to hospital late in the disease, we do not see nowadays the profound and continuing toxæmia, the gross extrauterine spread, and the multiple rigors of earlier years.

It is important to remember that the majority of anaerobic streptococcal infections are mixed infections (Butler and Hill, 1948), and in severe grades this may be

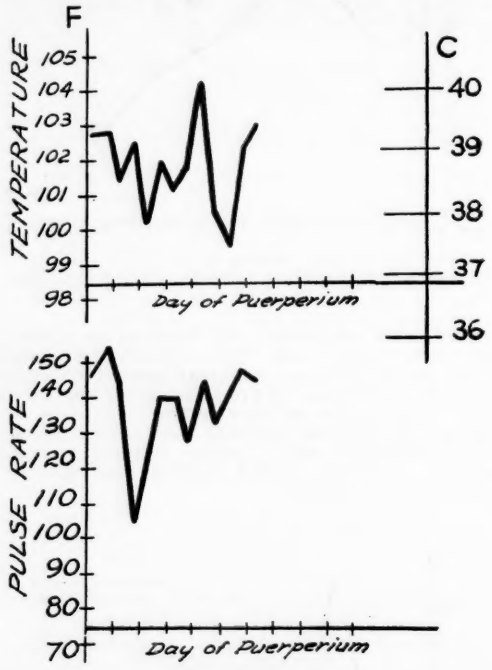

FIGURE VII.
Post-abortional septicæmia due to hæmolytic streptococcus group A, 1940.

an important cause of resistance to therapy, even with a combination of agents. It is likely, therefore, that an important place may come to be taken by a more recent antibiotic such as bacitracin, which has proved so valuable against mixed infections (Meleney *et alii*, 1949).

Figure III shows the chart of a patient with puerperal septicæmia due to anaerobic streptococci, who died in 1941. Figure IV is the chart of a patient with post-abortional general peritonitis due to anaerobic streptococci, who died in 1942. Figure V is the chart of a patient suffering from puerperal septicæmia due to anaerobic streptococci, who recovered with penicillin therapy in 1947.

Infections with Streptococcus Hæmolyticus Group A.

Infections with *Streptococcus hæmolyticus* group A should be the most easily preventible of all puerperal infections, for their source is entirely outside the genital tract. In Melbourne at present they comprise less than 5% of either abortional or puerperal infections. Their outstanding characteristic is high infectivity from case to case, a property shared with infections due to *Staphylococcus pyogenes*. The invasive ability of the bacteria depends on the virulence of the individual strain, not on lowered maternal resistance, and immediate smear examination of the vaginal swab, which can usually be completed within an hour, reveals the presence and the

virulence of the bacteria in a high percentage of cases (Butler, 1947). The speed and accuracy of this last investigation render it an invaluable aid to early and successful management and to the prevention of spread.

Control of infection depends, in its earliest phases, on proper ante-natal education; later, on correct face-masking, efficient antisepsis and asepsis, adequate facilities for the detection and treatment of carriers, for isolation of the patient, and for thorough sterilization and disinfection of

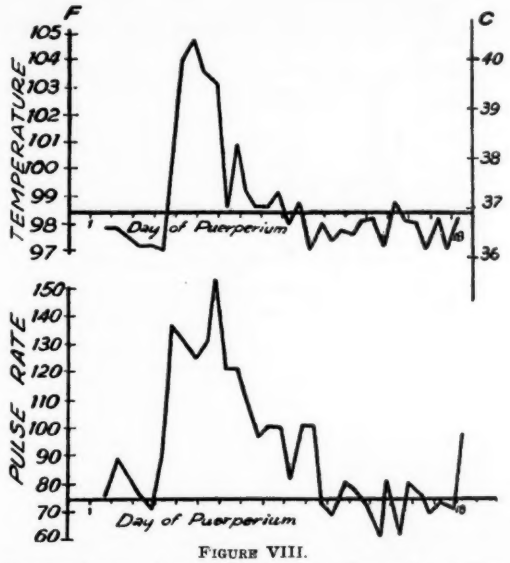

FIGURE VIII.

Puerperal general peritonitis due to hæmolytic streptococcus group A, 1946.

effects in contact with the patient; and lastly, on the susceptibility of the bacteria to sulphonamides or penicillin. As a result of these measures, deaths due to *Streptococcus hæmolyticus* group A infections have become very uncommon, but severe infections still occur, and such patients may prove difficult to save. At the Women's Hospital, since 1942, there have been one puerperal and two abortional deaths due to this cause, while in the immediately preceding three years there were two puerperal and eleven abortional deaths.

Although sulphonamides were responsible for the initial and outstanding improvement in the prognosis of these infections, considerably better results followed the introduction of penicillin, and it is our practice to employ it in all grave cases or whenever a satisfactory response to sulphonamides is not apparent within forty-eight hours.

Figure VI is the chart of a patient suffering from post-abortional general peritonitis due to *Streptococcus hæmolyticus* group A, who was admitted to hospital one week after uterine curettage, and died in 1940. Figure VII is the chart of a patient suffering from septicæmia due to *Streptococcus hæmolyticus* group A, who was admitted to hospital one week after abortion, and died in 1940. Figure VIII is the chart from a puerperal patient with early general peritonitis due to *Streptococcus hæmolyticus* Group A who responded to sulphonamide therapy in 1946.

Infections with Staphylococcus Pyogenes.

Although *Staphylococcus pyogenes* infections are not common, comprising less than 5% of puerperal or abortional infections in Melbourne, they have always been of great economic importance. This is due to the fact that although the majority of staphylococcal infections are mild, in a considerable proportion of the severer grades septicæmia occurs, and in past years has exacted a uniformly high mortality. Another important feature is the infectivity from case to case—a property evident in the well-known difficulty of eradicating staphylococcal infections from babies' nurseries (Knott and Blaikley, 1944), and also, as others have found, from obstetric units. No other obstetric infections have shown so dramatic a response to the introduction of antibiotics as have staphylococcal infections. Penicillin has proved life-saving, and its amazing powers are evident in Figure IX, a graph showing the yearly deaths from these infections during the past ten years.

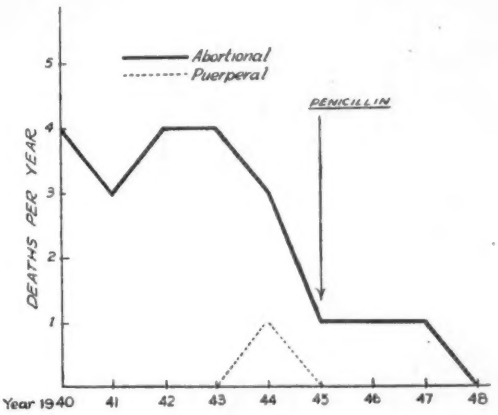

FIGURE IX.

Deaths due to infection by *Staphylococcus pyogenes*.

Still more striking evidence of the value of penicillin is shown in the records of proven cases of septicæmia due to *Staphylococcus pyogenes* over this period. In the five years prior to the use of penicillin there were 26 cases of septicæmia, with 16 deaths; in the five years following its introduction there were 22 cases of septicæmia, with three deaths.

Workers both here (Rountree and Thomson, 1949; Rountree and Barbour, 1950) and abroad (Barber *et alii*, 1949; Long, 1950) have stressed the dangerous tendency of staphylococci to develop drug resistance during treatment, particularly in public hospital practice, or when therapy is of inadequate concentration or of too short duration. Fortunately, we have been little troubled with drug resistance, no doubt because our patients do not acquire their genital staphylococci from hospital sources and therefore are not liable to be infected with resistant strains. With one or two exceptions we have thus obtained completely satisfactory therapeutic results with a penicillin dosage not exceeding 60,000 units every three hours. Should penicillin resistance develop, however, and not respond to increased dosage, the infection should be controllable by another antibiotic such as streptomycin, aureomycin or bacitracin, as first tested against the bacteria concerned.

The chart in Figure X is that of a patient suffering from septicæmia due to *Staphylococcus pyogenes*, who was admitted to hospital nine days after abortion and treated with sulphathiazole, and died in 1943. Figure XI is a chart from a patient suffering from post-abortional septicæmia due to *Staphylococcus pyogenes*, who was treated with penicillin and curettage and discharged from hospital in nine days, in 1949.

Infections with Clostridium Welchii.

Clostridium welchii infections appear to be particularly an Australian problem, and during the period under review were the commonest causes of abortional death in Melbourne. The source of the bacteria is the large bowel, and infection does not spread from case to case. The invasive ability of the bacteria depends on the virulence of the individual strain, not on lowered maternal resistance, although weak strains may multiply on devitalized tissue and produce toxin.

Clinically the grave infections due to *Clostridium welchii* are the most dramatic encountered in obstetrics and they present in three main forms: with rapidly progressive hæmolytic jaundice, with profound collapse, or with true uterine gangrene. Of enormous aid to early clinical diagnosis and correct management is immediate examination of the cervical swab, which reveals not only the presence and virulence of the bacteria but often the clinical type of infection (Butler, 1945).

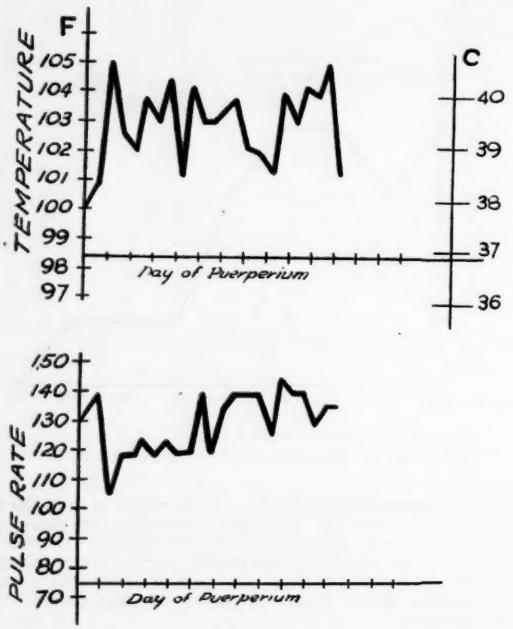

FIGURE X.
Post-abortional septicæmia due to *Staphylococcus pyogenes*, 1943.

In the last decade there have been one puerperal and 66 abortional deaths due to these infections, and all but 19 occurred prior to 1944. The major reason for this sudden and sustained fall in mortality has been the pronounced reduction in incidence of the severe forms of these infections, particularly of the "classical" hæmolytic infections, and also of potential infections as detected bacteriologically after the patient's admission to hospital. Additional factors are improved team work within the medical unit and between the medical and bacteriological units, greater speed and certainty in diagnosis and selectivity in treatment, and the introduction of penicillin.

The prognosis is most grave for patients with rapidly deepening jaundice, for once the patient has both exhibited deep jaundice and passed scanty, deep burgundy-coloured urine, the outlook is practically hopeless even though the blood is sterilized and the toxins are neutralized in a matter of hours. Fatal delay in making a diagnosis or in instituting therapy is here to be measured not in hours but in minutes. The immediate requirements are antitoxin (60,000 units given intravenously and 40,000 units intramuscularly, to be repeated every eight hours for twenty-four to thirty-six hours), penicillin (100,000 Oxford units given every three hours), copious fluids, alkalis, at times "Neosynephrin", uterine curettage, and perhaps later, when hæmolysis has been satisfactorily controlled, blood transfusion. The most important first needs are antitoxin, fluids and curettage, while penicillin is also of undoubted value because of its antibacterial action; in the fully-established infection, however, penicillin is unable to swing the balance towards recovery, and death from renal failure is usual.

In grave infections with collapse the same urgent concurrent measures are indicated, and here "Neosynephrin" administration and intravenous therapy are usually necessary to raise the patient's blood pressure to a satisfactory level for uterine curettage. Although the speed of progression to peripheral circulatory failure may be alarming in these cases, once therapy has been instituted the outlook is in general considerably more favourable than with established severe hæmolytic infection.

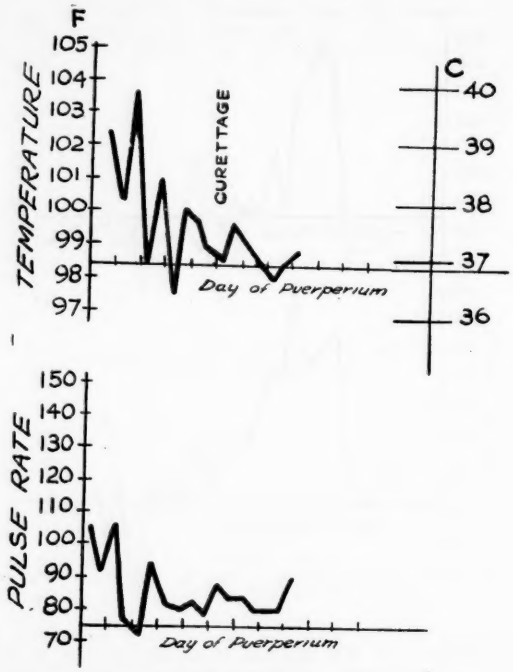

FIGURE XI.
Post-abortional septicæmia due to *Staphylococcus pyogenes*, 1949.

Of better outlook than either of the preceding examples of generalized infection are cases in which uterine damage is progressing to gangrene. These patients present with signs of peritonitic involvement localized immediately around the uterus, and with distinctive bacteriological findings. The time factor here is fortunately less urgent than in the severe generalized infections, for it usually takes something like forty-eight hours for severe uterine gangrene to be established. Prior to the introduction of penicillin, administration of antitoxin and hysterectomy were the basis of treatment, and provided the local or general disease was not too advanced when the patient was first examined or the condition first diagnosed, recovery could reasonably be expected. The use of penicillin has so greatly changed the picture that, when given sufficiently early, it both saves the patient and preserves her uterus, the only operative procedure required being early curettage to reduce the focus of infection; moreover, in infections so advanced that hysterectomy is essential the risks are immeasurably reduced.

The prevention of *Clostridium welchii* infections, which are almost entirely an abortional complication, is a social problem outside direct medical control. Medical management, as indicated, depends on the earliest possible clinical and bacteriological diagnosis and on the immediate institution of measures appropriate to the particular type of infection. Application of these principles over recent years has produced a considerable improvement in the outlook in certain types of this infection, but no general revolutionary change.

Discussion.

The outstanding cause of the profound changes in the face of obstetric infection in the last ten years has been the therapeutic efficacy of penicillin and to a much less extent that of sulphonamides. Employed sufficiently early, in adequate dosage, and with correct bacteriological and clinical indications, these agents will control the great majority of obstetric infections encountered today.

In at least 90% of cases penicillin is the agent of choice, sulphonamides being required chiefly for infections due to *Bacterium coli* and anaerobic Gram-negative bacilli; against the latter group, however, they are not uniformly effective.

We believe that in severe infections requiring penicillin it should be administered every three hours, longer intervals or the use of procaine penicillin being reserved for less severe infections. Our hospital routine is to give 30,000 Oxford units every three hours, the dose being increased to 60,000 units for moderately severe *Clostridium welchii* and severe staphylococcal or anaerobic streptococcal infections, and to 100,000 units for more resistant infections and for all severe *Clostridium welchii* infections. Heroic doses of 200,000 to 300,000 units are almost entirely reserved for cases of infective endocarditis.

In the field of prophylaxis these agents find their invaluable place in obstetrics associated with long-standing rupture of the membranes, in cases of prolonged labour, in the presence of a vaginal discharge, or when surgical measures are contemplated. Therapeutically they should be used for all severe and moderately severe infections, but in mild infections they are generally unnecessary unless there is some complicating factor such as a surgical wound, extrauterine spread, or the presence of bacteria infective to others (*Streptococcus hæmolyticus* group A, *Staphylococcus pyogenes*). Employed together with blood transfusions in infections following abortion, they have made immediate or early uterine curettage generally possible and have enormously reduced morbidity and stay in hospital.

Important disadvantages of penicillin are its need of parenteral administration for full efficiency, the development of penicillin-resistant strains, and the production by associated bacteria (for example, *Bacterium coli*) of neutralizing penicillinase. When these last factors cannot be overcome by massive dosage, other agents are required.

It is in such circumstances that some of the newer antibiotics may prove valuable and at times life-saving. The chief indication for their use is the presence of bacteria which are insensitive, resistant or antagonistic to penicillin and sulphonamides. Their main disadvantages are high cost, shortage of supply, an insufficient knowledge of their antibacterial capabilities, and in certain instances the development of toxic manifestations and drug resistance. For these reasons their selection should always depend on proven sensitivity of the bacteria concerned. With such indications, streptomycin may be employed against sulphonamide-resistant Gram-negative bacilli, aureomycin against penicillin-resistant cocci, and bacitracin in severe or resistant infections of mixed bacterial type.

It would seem that immediate improvement in the outlook of obstetric infections will depend less on increased efficiency in modern methods than on the development of more effective antibacterial compounds.

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TORSION OF THE TESTIS AND ITS APPENDAGES.[1]

By S. H. LOVELL,
Sydney.

TORSION of the testis and torsion of its appendages are clinical entities well known to all, but apparently not commonly seen. The word "apparently" is used deliberately, since it is believed that the condition is likely to be overlooked, and the main purpose of this paper is to discuss the subject briefly and to suggest a simple method of minimizing diagnostic errors.

The basis of this belief is the discrepancy between the frequency of the condition as expressed by figures published overseas and the apparent incidence in this country as expressed by such figures as are available to me. It is admitted that some of this discrepancy may well be due to the fact that some patients may not have been treated as in-patients, and only in-patient records are available. With this concession, the discrepancy is emphasized by the following figures. Abeshouse (1936) collected 156 cases, in addition to 194 cases collected by Muschat and Carp (1931). The local figures (Sydney) are as follows: Royal Prince Alfred Hospital, 16 cases; Royal Alexandra Hospital for Children, four cases; The Sydney Hospital, 10 cases. My own personal series consists of torsion of the testis six cases and torsion of the appendix of the testis four cases.

Further emphasis is given by the fact that Lambert and Smith were able to report four cases in a school of 650 boys in the period 1934-1935 and five cases in a school of 600 boys during the period 1933-1937.

These remarks lead to the first question: Do we recognize this lesion when we meet it?

My own interest in the subject was aroused by an encounter with three cases of torsion of the appendix of the testis occurring in close succession some twelve years ago. Since that date, questioning of students, resident medical officers, doctors and even holders of higher surgical qualifications has made it obvious that a goodly number have a very hazy idea of the subject and in particular of its pathology.

To some extent, this position may be explained on the basis of what is believed to be a faulty nomenclature —the term "torsion of the spermatic cord" is commonly used in text-books, and this is misleading.

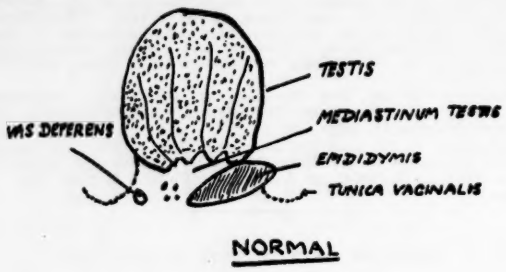
Some writers, including Young, have spoken of supravaginal or extravaginal and intravaginal torsions. No case has been recorded, to my knowledge, of extravaginal torsion, and I do not believe that it could ever occur. The torsion always occurs within the sac of the *tunica vaginalis* or, if descent is incomplete, the *processus vaginalis*.

[1] Read at a meeting of the Section of Surgery, Australasian Medical Congress (British Medical Association), Brisbane, May-June, 1950.

Pathology.

The second question is, therefore: What is the pathology of this condition?

This will be discussed initially under three headings: (i) Torsion of a completely descended testis. (ii) Torsion of an incompletely descended testis. (iii) Torsion of an appendage of the testis.



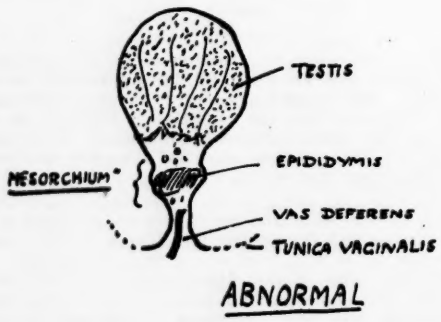


FIGURE I.

Torsion of a Completely Descended Testis.

Torsion of a completely descended testis never occurs with a completely normal testis—it occurs only when there has been a failure of consolidation of the *rete testis* resulting in a mesorchium which resembles a "mesentery" in its relation to the testis. This is illustrated in Figure I where such a development is compared to the normal. Such a testis is predisposed to undergo torsion at its mesorchium, quickly producing strangulation of the testis, followed by necrosis and atrophy. This is illustrated in Figure II.

Torsion of an Incompletely Descended Testis.

Torsion of an incompletely descended testis is commonly associated with an inguinal hernia and imperfect development of the testis, epididymis and cord, the testis being unusually mobile about its attachment to these latter structures, and it is about its attachment thereto that torsion may occur, with sequelæ already mentioned.

It is emphasized that torsion of the spermatic cord does not occur in either case, and it is felt that the term should be discarded.

Torsion of an Appendage of the Testis.

The appendage most commonly affected is the appendix of the testis, the so-called sessile appendage or hydatid of Morgagni. The other appendages—appendix of the epididymis, *vas aberrans*, and organ of Giraldes—are much less common structures, and torsion is particularly rare (Figure III).

General.

Before proceeding to discussion of the general pathology in explanation of the clinical features, I would stress my point that the term "torsion of the spermatic cord" is misleading and wrong. So far as I have been able to peruse the literature available here, there does not appear to have been a single case in which the cord, as we accept it in general speech, has undergone torsion. In his classic Bradshaw Lecture of 1928, Fagge, discussing the mechanism of torsions within the human body, referred to the principle of the screw and the nut. I might borrow this analogy, and thinking of the cord as the screw, say

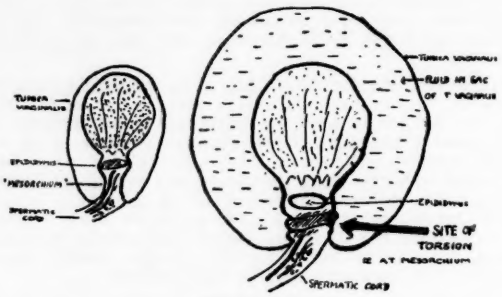


FIGURE II.
Torsion of the testis.

that I believe that, in this condition, it is always a case of the nut turning on the screw.

Further to support my belief that this accident does not occur in a completely normal testis, I draw attention to the fact that the great majority of cases occur in the second decade of life—that is, just after puberty when the testis is growing to its adult proportion. If this accident occurred in completely normal testes, one would expect it to occur more or less evenly throughout adult life. This is only indirect evidence admittedly, but it is very suggestive.

When pathological torsion occurs, the blood supply of the testis is occluded—the venous more or less completely and the arterial, in the first instance, partially. Very quickly the resulting œdema completes the occlusion of the arterial supply, and red infarction develops in the testis. While the testis is thus strangulated, and aseptic necrosis proceeds in the tissues which are the site of this red infarction, the surrounding tissues show the classical features of "aseptic" inflammation, in particular redness and œdema.

In the early stages, the *tunica vaginalis* contains a small quantity of turbid exudate, which, as strangulation proceeds, becomes sanguineous. In the absence of interference or of sepsis, the condition slowly subsides; the natural processes of tissue repair play their part in normal sequence until the necrotic testis, now virtually a foreign body, is replaced by a mass of fibrous tissue, recognizable from the exterior simply as an "atrophied testis".

Thus, in the established clinical state, we find one side of the scrotum (or inguinal area in the case of incompletely descended testes) showing some redness and œdema, with an injected *tunica vaginalis* containing blood-stained turbid fluid, in which lies an enlarged brown-blue-black enlarged testis and epididymis, twisted about its mesorchium.

The pathology of torsion of the appendages is similar in principle, but much more limited, although occasionally a surprising degree of œdema may be found in the adjacent cord. There is rarely any noticeable change in the testis or epididymis, and the fluid in the *tunica vaginalis* is usually only turbid. If the strangled appendage sloughs off, it may remain free in the cavity of the *tunica vaginalis* as a foreign body.

Clinical Features.

Most commonly pain is the first symptom. This is usually experienced in the scrotum, but in incompletely descended testes it may be inguinal or higher. Occasionally, there is no complaint of pain in the scrotum, although the testis is completely descended, but the pain

may be abdominal, suggesting an appendical condition or even, as in one case described in the French literature, a volvulus of the sigmoid colon.

There is usually some redness and œdema of the overlying scrotum (or other tissues) with tenderness. Sometimes this is the principal complaint made by the patient. Much is sometimes made of the suggestion that in torsion the position of the swollen testis *et cetera* is higher in the scrotum than in epididymo-orchitis, but this is not

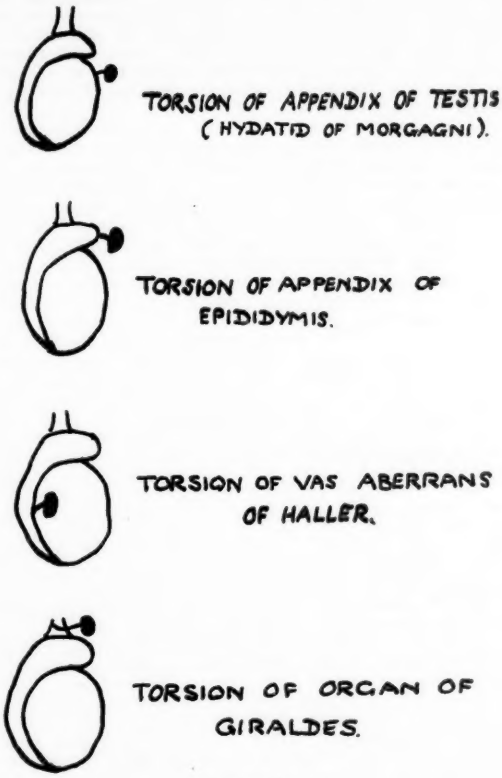


FIGURE III.

Torsion of appendages of the testis (after Dix).

necessarily the case. It would be true when torsion has occurred in an incompletely descended testis, but when the testis is a completely descended one, such elevation could occur only as a result of "cremasteric spasm". Some writers make no reference to this sign, while others stress its importance. My own opinion is that elevation of the testis would be accepted as a point in favour of the diagnosis of torsion, but the absence of elevation would certainly not bias me against such a diagnosis.

In view of the fact that the more complete the descent of the testis, the more likely it is to be a normally functioning one, it is the more important to save such a testis if it undergoes torsion, and not be misled by any absence of "elevation" in the scrotum.

The temperature is elevated, the average rise being to 99° to 101° F., but there is rarely any general constitutional disturbance, and urinary symptoms are rarely noted.

The above features are those noted in the typical case. Naturally, when an appendage has undergone torsion, the features are often less pronounced. In some instances, the torsion is undone spontaneously shortly after its development; such cases are the "*formes frustes*" described by Mouchet, whose writings in the French literature have contributed so greatly to our knowledge of this condition.

Incidentally, it is not uncommon to find that a patient with such a torsion will give a history of previous mild attacks of a similar nature, often occurring at night.

As mentioned earlier, the condition is most commonly found in patients between the ages of ten and twenty-five years, although it may occur at any age. The oldest in my own personal experience was thirty-two years of age. This patient is of some interest in that I was asked to see him in consultation because his "epididymo-orchitis" had not shown any improvement after five days of sulphadiazine treatment. He gave a history of previous attacks of mild pain in his testis (the left was the affected one), and most of these attacks had occurred at night. A diagnosis of torsion was confirmed at operation performed on the sixth day after the onset of the attack. Although the swollen testis and epididymis were blue-black, I performed an orchidopexy after undoing the torsion and made a number of small incisions in the *tunica albuginea* with the idea of accelerating the reduction of tension within the testis. With some surprise, I admit, I found that the condition quietly subsided and that without atrophy. When examined some two years later, he appeared to have a relatively normal testis and cord and incidentally had proved the efficiency at least of his other testis by having increased his family.

Now, if this condition occasionally is not recognized, with what do we confuse it? This is the third question, and the answer will be discussed under the heading of differential diagnosis.

Differential Diagnosis.

In many ways the condition simulates epididymo-orchitis, sometimes very closely. This resemblance may be more misleading since it is now more commonly accepted that many cases of epididymo-orchitis are not of gonococcal origin. A little extravagance may be pardoned to press home a point, and it may be said that any case of "epididymo-orchitis" which is followed by atrophy was probably a missed case of torsion.

This is the real difficulty in diagnosis in the acute and typical case. Occasionally it may be confused with a tuberculous condition, or a tumour, and with an undescended testis it may simulate an incarcerated or strangulated hernia. Thrombosis of the cord, a rare entity, may result in a clinical condition closely resembling torsion. For some years it has always been my practice to examine the scrotal contents carefully as part of my routine abdominal examination, particularly in cases of "acute appendicitis".

In some of the milder cases, particularly when the torsion affects only the appendages, and the symptoms are referred to the abdomen, the presence of a small, tender swelling in the scrotum may be overlooked, as happened in the case mentioned previously—here a child was referred for fixation of his sigmoid for recurring volvulus when, in fact, the cause of his pain was a torsion of a hydatid of Morgagni.

It will be appreciated from these remarks that in differential diagnosis the most important thing to do is to keep the existence of this clinical entity in mind, and that, in brief, is the answer to the third question: Why might we fail to diagnose it?

The fourth and final question follows as a corollary to the answer just given: If we suspect it what can we do? The answer is provided in the following paragraph.

Treatment.

Whenever the diagnosis is suspected and when a diagnosis of epididymo-orchitis is not unmistakably correct, with the patient under anæsthesia make a transverse incision over the scrotal tumour, open the *tunica vaginalis* and inspect the testis. This procedure is particularly simple and can be done very well with the patient under intravenous anæsthesia. If torsion has occurred it will be abundantly obvious even to one who had never seen the lesion previously, and it can be dealt with easily. If, on the other hand, it is a case of epididymo-orchitis, the wound can be closed and no harm will result. It is felt that this procedure should be followed in any doubtful

case—this is the only way to be sure, it is the only way to minimize the risk of atrophy of a testis which might have been saved, and it is so easy. This is the point this paper seeks to stress.

Some speak of external manipulation; this might be successful, but surely in the light of the pathology described, recurrence must be expected, and there appears to be no justification for failing to operate once the condition is diagnosed. The possibility of a bilateral condition should also be remembered.

Some speak of inguinal incisions, but surely it is simpler to approach the lesion by the most direct route. Naturally, an inguinal incision will be called for when the testis is incompletely descended and lying in the inguinal canal, but when its descent is complete this is considered to be unwise.

When the diagnosis of torsion has been confirmed at operation, it is probably quite safe to undo the torsion and perform some form of orchidopexy within the *tunica vaginalis*. Orchidectomy should be reserved for cases of several days' standing with an obviously necrotic sloughing testis. In one case I have had to carry out a secondary orchidectomy following an attempted orchidopexy. I also consider that it is a good plan to make multiple small incisions in the *tunica albuginea* as mentioned in the cases I have described. This can do no harm, and it may accelerate the reduction of tension within the testis in border-line cases. This procedure, by the way, may also prove of value in cases of mumps orchitis, since the atrophy in such cases is probably due only to the vascular occlusion caused by the great increase of tension within the *tunica albuginea*. It is also erring on the safe side to drain the sac of the *tunica vaginalis* by a small tube for twenty-four to thirty-six hours. Post-operatively, chemotherapy may be used in a prophylactic role, although it hardly seems necessary.

In cases occurring in incompletely descended testes, the operative procedure is the same, but no attempt should be made to deal with a hernia sac should it coexist—this can be disposed of at a later operation.

When torsion of an appendage is found on the opening of the *tunica vaginalis*, the strangled appendage is nipped with scissors, and if there is any oozing from the base, this can be controlled by a single mattress suture of fine plain catgut. A little penicillin-sulphanilamide powder may be dusted over the testis and the wound closed in layers without drainage.

Thus the fourth question is answered, and the answer may be emphasized by quoting Mouchet, who contended twenty-odd years ago that "all cases of primary inflammation of the scrotal contents occurring about the age of puberty should have the benefit of surgical intervention". Since the literature contains records of cases occurring at other times from the first year of life onwards, this benefit might well be conferred on other patients whose diagnosis of "epididymo-orchitis" is not beyond doubt, and this appears to be the only reasonable way to minimize diagnostic errors.

HEPATITIS: TREATMENT WITH BREWER'S YEAST.

By NEVILLE DAVIS, M.B., Ch.M.,
Sydney.

CIRRHOSIS of the liver, or Laennec's disease, has long been recognized as a clinical entity with symptoms and physical signs that are unmistakable. Its prognosis was most unfavourable, and its treatment entirely palliative. The recognition of the disease rarely occurred before the manifestation of hepatomegaly, ascites and hæmatemesis. The termination of the illness usually took place within a year of the appearance and recognition of one or all of these symptoms. Many workers and clinicians had believed that it should be possible to diagnose this disease before it reached the hopelessly incurable stage. The terms "subacute" or "chronic hepatitis" and "hepatic insufficiency" had been used to describe the various stages of the disease. It remained, however, for Patek and his co-workers in 1937 and 1939 (Patek, 1937; Patek and Post, 1941) to give a clearer clinical picture, and to suggest a different ætiology and a more rational treatment.

Post-mortem studies had shown injury and necrosis of the liver parenchyma with the replacement of the delicate liver cells by fibrosis. Cirrhosis of the liver had previously been associated with an alcoholic ætiology, and frequently coupled with a syphilitic background. Workers at the Mayo Clinic, led by McCarthy, had demonstrated in the post-mortem room pronounced cirrhosis of the liver in patients who had never taken alcohol throughout their life and who also had denied the acquisition of syphilis. Their blood had repeatedly failed to give the Wassermann reaction.

Patek advanced the theory that liver damage which resulted in cirrhosis of the liver was due to a nutritional deficiency, and that liver cells could be protected during the period of reversionary changes in the cells, by the administration of vitamin *B* and a diet of high protein and carbohydrate content and low fat content. Experimental studies had shown that liver cells were damaged by the action of various hepatotoxic agents. When these agents acted in large doses cellular necrosis occurred with resultant acute cirrhosis. When these same toxins operated in smaller amounts, but more frequently, the result was a more chronic hepatitis, and a definite hepatic insufficiency in the earlier stages. Experimentally, György and Goldblatt (1949) showed that the liver cells could be damaged by a diet of low protein (casein) content and high fat content. It had been recognized for many years that proteins could protect liver cells and neutralize the action of hepatotoxins. Best and his co-workers (Best and Lucas, 1943) had also shown that choline and methionine had "lipotropic" activity of a protective character, whilst cystine in the nature of free amino acids had a deleterious action on liver cells. The influence of the tocopherols in vitamin *E* on liver cells is still in doubt, but the weight of evidence favours its beneficial action in the prevention of cellular necrosis. However, there is now general agreement that fats and cod-liver oil should both be used sparingly when liver damage is believed to have occurred. György and Goldblatt have recently stated that the œstrogenic and goitrogenic hormones retard the onset of hepatic cellular damage. It is extremely likely that the combined actions of diet and œstrogenic hormones play an important part in liver damage associated with the toxæmias of pregnancy. More attention could with advantage be given to a carefully studied diet in the post-parturitional states when there has been toxæmia of pregnancy. Furthermore, attention to a properly arranged diet of high protein and carbohydrate and low fat content, with large doses of vitamin *B* during the months of pregnancy, could be a factor in the prophylaxis against the onset of toxæmia of pregnancy.

Treadwell in 1944-1945 suggested the addition of methionine to the high protein content in the diet. It does not in any way remedy protein deficiency, but its action is reinforcing in character and lipotropic in effect.

There is considerable conflict of opinion on the relative value of tests for liver insufficiency. The variation from normal in these tests has provided the basis of diagnosis in the early recognition of subacute hepatitis or liver insufficiency. Before consideration of the relative value of these tests it is essential to recognize a syndrome of symptoms associated with the early onset of this disease. These symptoms are as follows: (i) loss of energy and fatigue, more noticeable on awakening than during the rest of the day; (ii) epigastric fullness, belching, diminished appetite, dislike for fat, eructation of gas, and nausea; (iii) stools either constipated or loose, but rarely normal; (iv) a dull ache in the right upper quadrant of the abdomen without muscular rigidity; (v) dizziness and giddiness, sensation of heat and burning over the body, also a dull, persistent headache (not relieved by aspirin or its derivatives); (vi) a feeling of depression, with poor mental concentration; (vii) the presence of hæmorrhoids, which may bleed or protrude and frequently are the seat of thrombosis.

These symptoms may occur in any order or in any combination. They may simulate gastric neurosis, subacute gastritis, chronic cholecystitis without calculi, early leuchæmia, and post-parturitional states consequent upon toxæmia of pregnancy.

Tests for liver function are numerous, and there is a wide divergence of opinion as to their relative significance and value. Bilirubin in the urine, with excess of this substance in the serum, presages definite liver damage. The bromsulphalein test is of great value in diagnosis: an estimation of 4% after forty-five minutes, or of 3% at the end of one hour, may be considered as abnormal. Alteration in the serum albumin-globulin ratio is important. In active hepatitis the serum albumin level falls and the serum globulin level rises. The hippuric acid excretion test supplies valuable information; the result can be determined as a percentage of normal after the oral administration of four grammes of sodium benzoate in solution. The estimation of serum cholesterol and the galactose test are also helpful in the estimation of liver cell damage. Not any, or all, of these tests, however, tell the degree of liver cell damage or the amount of liver insufficiency that has developed. Liver puncture as a means of diagnosis gives infinitely more exact diagnosis, but it is not unattended by danger, with a possible fatal result. The technique and interpretation of the test are still difficult, and it should be used only by highly specialized and trained people.

Since 1942, 126 patients with acute or subacute hepatitis have been under treatment in the present series of cases. The diagnosis of the clinical entity has been confirmed by the performance of the tests for liver insufficiency and also, when necessary, radiologically through the Graham test. The biochemical tests in use in this series of cases have been hippuric acid excretion, galactose estimation, and serum cholesterol estimation.

Cases of advanced cirrhosis of the liver, with pronounced hepatomegaly, ascites *et cetera* have not been included in this series, for the reason that an endeavour has been made to evaluate the treatment of patients with early acute and subacute hepatitis, and also to emphasize the importance of early diagnosis. Of the 126 patients, 54 were females and 72 males. Seven of the 54 females became pregnant whilst under treatment. In each case they were delivered of a live baby at full time, without any undue symptoms of toxæmia of pregnancy. When each patient came under observation, liver function tests (galactose estimation, serum cholesterol estimation and hippuric acid excretion) were carried out, and these were repeated at intervals of three to six months through treatment. The patients were divided into three grades, according to the degree of liver insufficiency estimated by means of the liver function tests at the initial examination. These grades were as follows:

Grade 1: those whose liver deficiency was greater than 50%.

Grade 2: those whose liver deficiency was more than 25% and less than 50%.

Grade 3: those whose liver deficiency was more than 10% and less than 25% (the early cases).

Table I shows the number of years the patients were under treatment, and also the number of patients in each of three grades. The average age of the patients was forty-two years at the beginning of treatment.

Treatment.

Uniform treatment was instituted in all cases. Details are as follows.

Rest.—In the severe cases (19) the patients were put to bed at rest for a period of four to six weeks. All other patients were allowed to carry on their duties without interference.

Diet.—All were given a diet of high calorie content consisting of 140 grammes of protein, 350 to 400 grammes of carbohydrate and 70 grammes of fat. To this diet was added vitamin *B* complex consisting of a daily dosage of 30 milligrammes of B_1, five milligrammes of riboflavin, and 25 milligrammes of niacin. Neither choline nor methionine was included in the diet.

Brewer's Yeast.—All patients were given dehydrated brewer's yeast, 12 grammes daily. This was given during each meal, dissolved in barley water, milk or fruit juice. The brewer's yeast was dehydrated and prepared by the Compressed Yeast Company, who made available stocks for the purposes of this research. Independent analyses of the dehydrated brewer's yeast were made by A. Bolliger and N. T. Hinks, of the Gordon Craig Research Laboratory (University of Sydney). The result of the analyses showed 12·5 milligrammes *per centum* of thiamine (B_1) and 7·0 milligrammes *per centum* of riboflavin (B_2).

TABLE I.
(126 Cases.)

Number of Years under Treatment.	Number of Patients.			
	Total.	Grade 1.	Grade 2.	Grade 3.
8	7	3	2	2
7	3	0	2	1
6	8	0	7	1
5	17	3	4	10
4	35	3	14	18
3	33	7	13	13
2	10	2	4	4
1	10	1	6	3
Less than 1 year	3	0	2	1
Total	126	19	52	53

Sedatives.—Some of the more excitable patients were given sodium phenobarbital (0·5 grain) three times daily.

Results of Treatment.

The patients were arbitrarily graded into groups of "cured", "improved", "relieved" and "unchanged". The "cured" group consists of those patients the results of whose liver function tests returned to normal, and whose symptoms entirely disappeared. Those patients whose symptoms disappeared, and the results of those liver function tests improved, but did not become normal, were classified as "improved"; whilst those whose symptoms decreased, but who showed little variation in the results of liver function tests, were graded as "relieved". One patient (aged seventy-seven years) died of cerebral hæmorrhage one year after the beginning of treatment.

Table II shows the results of treatment.

TABLE II.

Number of Years under Treatment.	Results.				
	Cured.	Improved.	Relieved.	Unrelieved.	Died.
8	2	4	1	0	0
7	0	0	3	0	0
6	4	3	1	0	0
5	4	6	7	0	0
4	8	8	17	2	0
3	7	12	11	2	1
2	2	3	5	0	0
1	2	2	6	0	0
Less than 1 year	0	2	1	0	0
Total ..	29	40	52	4	1

Summary.

1. The early diagnosis of hepatic disease (hepatitis) is extremely important as regards the prognosis and early institution of treatment.

2. The value of diet is emphasized. A diet of high calorie content is necessary and should have a high protein and carbohydrate content, with a low fat content.

3. Dehydrated brewer's yeast containing a high percentage of vitamin *B* is of definite assistance in treatment.

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IMMUNIZATION AGAINST TUBERCULOSIS IN AUSTRALIA AND NEW GUINEA.[1]

By E. A. NORTH, M.D. (Melbourne), M.R.A.C.P.,
Commonwealth Serum Laboratories, Melbourne,

AND

D. JAMIESON, F.R.F.P.S., M.R.C.P. (London), B.Sc., D.T.M. and H.,
Department of Public Health, Papua and New Guinea.

(From the Commonwealth Serum Laboratories, Melbourne.)

IN practice, immunization against tuberculosis means inoculation with living B.C.G. (*Bacille Calmette-Guérin*). At present its only possible rival is the vole bacillus (Wells, 1946), which recently has been shown to afford a high degree of temporary protection against tuberculosis in cattle (Young and Paterson, 1949). However, proof that it will raise the resistance of humans against tuberculous infection is still lacking.

B.C.G. has had a very chequered career since Weill-Hallé first administered it to infants in 1921. Calmette's early claims were soon severely questioned on the grounds that his work was not properly controlled, while some critics maintained that the vaccine was actually dangerous. A bitter controversy developed between Calmette and Petroff, who claimed that he had isolated pathogenic variants from a culture of B.C.G. At the height of this dispute the Lubeck disaster occurred and Calmette's vaccine became largely discredited outside France.

However, during the period of eclipse, Scandinavian workers had been studying the subject from a somewhat different angle. One of the foremost was Heimbeck, who first showed that student nurses who did not react to tuberculin were prone to develop clinical tuberculosis during their training. His claim that he had increased their resistance with B.C.G., and that this increased resistance ran parallel with the development of bacterial allergy, has been confirmed by Ferguson (1946) in Canada.

Others who laid the foundations for the modern concepts of B.C.G. vaccination include Wallgren, a Swedish pædiatrician of international reputation, who independently of Heimbeck introduced the intradermal method of vaccination, and K. A. Jensen, of Copenhagen, who studied both the laboratory and the clinical aspects.

Within the past few years progress results of several long-term controlled studies in North America have been published, which fully confirm the experience of the Scandinavians.

The significance of recent evidence in favour of B.C.G. has been fully appreciated in Australia. At the Plenary Session of the Sixth Session of the Australasian Medical Congress (British Medical Association), held in Perth in August, 1948, the use of B.C.G. was advocated by several speakers as one method for the prevention of tuberculosis.

[1] Read at a meeting of the Section of Public Health, Tuberculosis, Tropical Medicine and Industrial Medicine of the Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

Then at a combined meeting of the Section of Pathology, Bacteriology, Biochemistry and Experimental Medicine and the Section of Public Health, Tuberculosis and Tropical Medicine at the same Congress, Dr. D. R. W. Cowan (1948) read a paper on the clinical aspects of B.C.G. vaccination and the need to protect "Mantoux-negative" nurses against the effects of primary tuberculous infection. He reported on more than 500 vaccinations carried out by the multiple puncture method with vaccine prepared in Adelaide, and stressed the fact that vaccination was offered as an addition to, not as an alternative to, other methods of control.

About the same time vaccine flown in from Canada was being used in general hospitals and sanatoria in Victoria (Ebbs, 1948), and towards the end of 1948 B.C.G. vaccine became available for general distribution from the Commonwealth Serum Laboratories.

Acting on the recommendation of the National Health and Medical Research Council, the central health authorities in the different States have, for the time being, accepted the responsibility of controlling the use of the vaccine. At present B.C.G. vaccine is being made available to protect those of "Mantoux-negative" status who are either living or working in a potentially highly infected environment, particularly trainee nurses and children in infected households.

RELATIONSHIP OF BACTERIAL ALLERGY TO IMMUNITY.

The intradermal method of vaccination has been adopted here, and reports so far indicate that in general high Mantoux conversion rates are being obtained even in distant centres. There is evidence that production of sensitivity to tuberculin is an important criterion for determining whether or not immunity has been enhanced by the procedure (Aronson and Palmer, 1946; Heimbeck, 1947). Further, Birkhaug (1944) and Holm (1946) consider that the effect of vaccination lasts only so long as the positive tuberculin reaction persists. Their view is upheld by most B.C.G. workers, but unfortunately there is no direct evidence on the point.

Jacox and Meade (1949) have found a remarkable difference in the durability of the allergy following the use of two vaccines prepared in different laboratories, although with each the immediate Mantoux conversion rate was high. They conclude that if, as is believed, sensitivity is a reflection of immunity, a suitable method of control of the sensitizing potency of B.C.G. vaccine should be set up.

Unfortunately, because a completely reliable drying technique is not yet available, vaccination with B.C.G. vaccine has to be performed before all the necessary testing of the vaccine has been completed. For the same reason there is no international standard for comparison, but the Expert Committee on Biological Standardization of the World Health Organization has laid down certain requirements for laboratories engaged in the preparation of B.C.G. vaccine for the United Nations International Children's Emergency Fund (U.N.I.C.E.F.) Vaccination Campaign.

However, such requirements cannot ensure uniformity of antigenicity, and the assay of B.C.G. vaccine must for the present remain essentially a clinical one, depending on Mantoux testing and the local reaction at the site of inoculation. Table I shows part of the protocol of a typical assay which is carried out on each batch by Dr. Dorothea Church, of the Central Tuberculosis Bureau, Melbourne.

If the results of B.C.G. vaccination, as judged by Mantoux testing, are to be comparable, the test used must be standardized. The standard suggested is the injection of 10 tuberculin units—that is, 0·1 milligramme of old tuberculin (0·1 millilitre of 1:1000 dilution) or 0·0002 milligramme of purified protein derivative—with an area of infiltration at least five to six millimetres in diameter after forty-eight to seventy two hours as the criterion of a positive reaction. We have adopted this procedure as a routine, but results here obviously will not be comparable with those of workers who test with 1·0 milligramme of old tuberculin (Holm, 1946; Jacox and Meade, 1949), or who accept an area of erythema without infiltration as a positive response (Jacox and Meade, 1949).

We have called attention to this lack of uniformity because many people tend to accept reports of Mantoux conversion rates and durability of allergy following B.C.G. simply on their face value. We believe that in the present unsatisfactory state of knowledge we must endeavour to produce a durable allergy, particularly when the infection rate is low. In a very highly infective environment, early accidental superinfection will act as a secondary stimulus and enhance and prolong the resistance indefinitely.

TABLE I.

Clinical Assay B.C.G. Vaccine: Batch 96.[1]

Identity.	Age. (Years.)	Sex.	Mantoux Reaction.[2] (Millimetres.)	Local Lesion.
M.A.	4	F.	I. 20 E. 40	
A.A.	8	F.	I. 17 E. 40	No ulcer.
J.A.	4	F.	I. 15 E. 50	No ulcer.
T.A.	1½	F.	I. 15 E. 30	Small ulcer.
A.D.	1½	M.	I. 15 E. 40	Scab 10 mm.
M.D.	3	F.	I. 20 E. 60	No ulcer.
O.R.	6	M.	I. 15	Scab 6 mm.
F.B.	9	M.	I. 15 E. 40	Scab 8 mm.
P.B.	15	F.	I. 20 E. 50	Scab 7 mm.
R.O'N... ..	10	F.	I. 15 E. 50	Scab 4 mm.
W.O'N. ..	8	F.	I. 15 E. 50	Ulcer 7 mm.

[1] Vaccine prepared February 1, 1950; vaccination carried out February 9, 1950; Mantoux test carried out April 4, 1950; total number in assay, 30; reactions read by Dr. D. Church.

[2] "I."=diameter of area of infiltration (average 16 millimetres); "E."=diameter of erythematous area.

It is too early yet to know whether we are producing a sufficiently durable allergy with B.C.G. in Australia. A "sufficiently durable allergy" is a vague term, but in general we mean an allergy that will at least last during the training period of nursing and medical students. A research into ways of prolonging the post-vaccination sensitivity to tuberculin is at present being undertaken in Melbourne.

TUBERCULOSIS AMONGST PRIMITIVE RACES IN THE SOUTH PACIFIC.

The incidence of tuberculosis amongst most of the indigenous peoples in the South Pacific is difficult to assess; but what is known concerning it is disquieting (North, 1949). These peoples include our own Australian aborigines and the natives of New Guinea (Australian and Dutch), the Solomons, the New Hebrides, New Caledonia, the Gilbert and Ellice Islands, New Zealand, Fiji, Samoa and Tahiti.

In New Zealand the tuberculosis mortality rate among Maoris is at least ten times greater than among Europeans, although the incidence of the disease amongst the former is only about five times higher. Therefore tuberculosis is not only more prevalent but also more lethal in the Maori than in the white man. In 1947 there were 28 deaths from tuberculous meningitis amongst approximately 100,000 Maoris, compared with 16 amongst the 1,700,000 Europeans in New Zealand—a proportion of nearly 30 to 1 (Taylor, 1948).

In Fiji the tuberculosis death rate was recently stated to be 159 per 100,000 amongst the indigenous Melanesians, compared with 34 per 100,000 amongst the Indians there, but as most cases notified from the country areas were unconfirmed by laboratory or X-ray examination, the exact incidence of tuberculosis was in doubt (Snodgrass, 1947).

An international body, the South Pacific Commission, whose functions include research into and advice on measures to improve the well-being of indigenous populations, has recently been set up by the nations with territories in this area (Britain, France, Holland, United States of America, Australia and New Zealand), and it is significant that there is a link between the South Pacific Commission and the World Health Organization. The member for health on the Research Council of the Commission, Dr. E. Massal, considers tuberculosis a major health problem throughout the whole area, and already he has a research team studying methods for individual diagnosis of the disease under field conditions. He proposes next to conduct epidemiological surveys in the different countries using the information already gained, and finally, when adequate data are collected, to organize research into methods for controlling the disease.

The spectacular results following B.C.G. vaccination of North American Indians (Oronson, 1948; Ferguson and Simes, 1949) afford grounds for believing that specific immunization will play its part in controlling tuberculosis amongst indigenous Pacific peoples. B.C.G. vaccine is now being dispatched regularly by air from Melbourne to New Zealand, Fiji and North Queensland.

Dr. A. Fryberg, the Director-General of Health for Queensland, and Dr. E. W. Abrahams, the Director of Tuberculosis, are concerned about the incidence of tuberculosis amongst aborigines in the Cape York Peninsula and Torres Strait islands, where Dr. Macken has been studying its epidemiology and carrying out vaccination. All this experience together with that gained in New Guinea should prove valuable to the Commission's Research Council.

THE PROBLEMS OF TUBERCULOSIS AND ITS CONTROL IN PAPUA AND NEW GUINEA.

Tuberculosis has existed for many years amongst the natives of New Guinea, mainly around centres of European population along the coasts. In the Rabaul area, for instance, it was reported nearly twenty-five years ago that whilst only 5% of labourers were "Pirquet-positive" when they arrived from their villages, 40% reacted to tuberculin one year later, whilst autopsy showed that nearly 25% of all deaths amongst indentured labourers were due to tuberculosis (Cilento, 1926).

The Port Moresby area has long been known to be badly infected and the disease usually is rapidly fatal. Practically all the adult population of Hanuabada, a village close to Port Moresby, were recently found to be "Mantoux-positive" (Lancaster and Jones, 1948).

On the other hand, little or no tuberculosis exists in places where the Melanesian is living his own life free from contact with the white man. Up to the time when the work recorded below was undertaken, the central highlands were regarded as being completely "unseeded". This region is almost completely cut off from communication with the outside world except by aircraft. The climate is good, the soil in the valleys is very fertile, and the native population is large and virile.

In the coastal areas there is a serious shortage of manpower and the Administration has been forced to adopt a policy of recruiting short-term indentured labourers from the highlands. Thus Dr. J. T. Gunther, the Director of Public Health, now has the urgent problems of (i) protecting the labourers proceeding to the coast, (ii) preventing them from acting as "spreaders" on their return, and (iii) controlling the disease in areas already heavily infected.

Facilities for putting orthodox methods of prevention into practice in the immediate future were so limited that mass immunization with B.C.G. offered the only reasonable prospect of meeting the challenge.

It was decided that priority be given to the central highlands, and the B.C.G. campaign started there in

December, 1949. The planning of such a campaign falls naturally under three headings: (i) Mantoux test surveys of all areas to ascertain the incidence of tuberculosis and the probable routes of spread; (ii) organization of B.C.G. inoculations; (iii) examinations for Mantoux conversions and states of local reaction.

B.C.G. Immunization in Papua and New Guinea.

The central highlands district is situated at about 5000 feet above sea level, is very mountainous and was penetrated by the white man only within the past twenty years; there are still only a handful of Europeans there.

If, as was believed, the highlands were completely unseeded, routine Mantoux testing prior to vaccination would be unnecessary. Even if a few persons were already infected and it was known that B.C.G. would cause them little inconvenience, omission of the preliminary test might still be justifiable.

Again, if it was known that in a mass campaign a 98% to 99% Mantoux conversion rate could be relied on, if a particular vaccine and technique were used, only a selected group would need testing after vaccination—as a check on the vaccine and methods used in administering it (Holm, 1948).

The results now reported were mostly obtained in the course of investigating these points and mainly concern the highlands. Epidemiological surveys in the Trobriand Islands and in the Port Moresby area are included to complete the picture.

Materials and Methods.

The peoples and areas covered in the investigation will be referred to later.

Mantoux Tests.—The Mantoux tests were carried out as follows. A dose of 0·1 millilitre of a freshly prepared dilution of old tuberculin in normal saline (1:1000 unless otherwise stated) was used. Reactions were read after forty-eight hours and graded as follows: "+", an area of infiltration of maximum diameter 5 to 10 millimetres; "++", an area of infiltration of maximum diameter 11 to 20 millimetres; "+++", an area of infiltration of maximum diameter over 20 millimetres; "++++", an area of infiltration with vesiculation or necrosis.

Modified Koch Reaction following B.C.G. Vaccination in Subjects Already "Mantoux-Positive".—Reactions were read forty-eight hours after the intradermal injection of 0·1 millilitre of B.C.G., which was given at the same time as the tuberculin for the Mantoux tests. The reactions were graded as for the Mantoux tests.

B.C.G. Vaccine.—The B.C.G. vaccine used was the standard vaccine as used in Australia, and contained 0·5 milligramme (semi-dry weight) of B.C.G. per millilitre. It was dispatched from Melbourne to Lae by air and transhipped by chartered aeroplane from there to the highlands. The actual time of air travel would normally be less than twenty-four hours. As far as was possible the vaccine was refrigerated when not actually in transit. It was used six to ten days after preparation. The effect of delays in transit is dealt with later. The dosage of vaccine was 0·1 milligramme given intradermally over the left deltoid region.

Identification and Control of Those Vaccinated.—1. A roll is called from the village book, in which are recorded the names, ages, sexes *et cetera* of all the people therein. A stamp is placed opposite the names of those vaccinated.

2. A tattoo with a single intradermal injection of a 1 in 20 dilution of indian ink in carbolized normal saline is made three inches above the left olecranon process.

3. A list is taken of all persons injected, with details of age, sex *et cetera*.

Results.

Experienced B.C.G. workers have found that there is no danger in vaccinating individuals who are already reactors to tuberculin, even those with active lesions. The greater tendency to ulceration and excessive scarring, and the fact that such vaccination is unnecessary and tends to confuse results, are good reasons for not doing so, especially in Europeans. Small ulcerations and other local reactions do not worry the New Guinea natives.

The harmlessness of giving simultaneous injections of B.C.G. in the deltoid region and of tuberculin in the forearm was first confirmed on one of ourselves and then on a small number of natives under constant medical observation in Port Moresby.

The reactions to B.C.G. compared with those to tuberculin in station natives at Goroka are shown in Table II. Similar results were obtained at Mount Hagen and Kainantu. Later observations indicated that if the reactions had been read at seventy-two hours the correlation would have been much closer.

The degree of ulceration that resulted was greater than in "Mantoux-negative" subjects, but was never serious. All ulcers had healed within twelve weeks.

Mantoux Test Surveys.

The areas covered are shown in the accompanying sketch map of Papua and New Guinea (Figure I).

The central highlands surveys were carried out in the four main areas, Kainantu, Goroka, Chimbu and Mount Hagen. There is no vehicular road between any two of them at present, but Kainantu, at the head of the Markham Valley, is the least isolated from the coast.

In each area there is an administrative station with a small European staff and their families and some hundreds of station natives (police, hospital orderlies and labourers and their families) and prisoners from the surrounding district. Some station natives, mainly police, are from the coast; a few others had had known coastal contacts.

Prior to the war an official permit was required before a coastal native could enter the highlands.

The true indigenes live in villages, hamlets or family groups throughout the area. The terrain is such that it may take a medical unit days to reach a village thirty miles or so from the station.

The Trobriand Islands are a group of coral islands situated in the south-east part of the territory. The people are Papuo-Melanesian. They have long been visited by the white man, but owing to their remarkable beliefs have migrated little from their own islands.

The only other area extensively surveyed was Tatana village, six miles from Porth Moresby, but in close contact with it. The natives there are typical Papuans.

TABLE II.

Reaction to Tuberculin Compared with Reaction to B.C.G. in Station and Village Natives at Goroka.[1]

Reaction.	Total Number Injected.	Number Reacting.				Total Positive Reactors.	Total Number with an Area of Over 19 Millimetres, Infiltration (++, +++ and ++++),.
		+	++	+++	++++		
Mantoux	633	15	19	16	5	55	40
Koch	633	37	18	18	4	77	40

[1] All received 0·1 millilitre of 1 in 1000 old tuberculin intradermally in the left forearm and 0·1 millilitre of B.C.G. vaccine in the left deltoid area at the same time, and the reactions were read two days later.

Two other areas, Kikori and Higaturu, must be mentioned, as they are referred to later. The former is a swampy coastal village situated some days' journey east of Port Moresby, and the latter a subcoastal area north-east of Port Moresby.

Central Highlands Survey.—The results of the central highlands survey are shown in Table III. The most striking feature of this table is the very low reading for all village natives. The highest reading is found at Kainantu, the gateway to the highlands. The relatively high incidence

FIG. 1. PAPUA AND NEW GUINEA.

FIGURE I.
Papua and New Guinea.

among natives who have had coastal contacts is interesting, but the increase in incidence among natives employed on stations is remarkable. The increase is sometimes as much as eighty-fold. One can also, in the Goroka area, trace a falling gradient of incidence as one moves from the station. The European population has been subject to a careful medical examination, and the number of coastal natives is not large. Many of the latter are picked specifically for their physical fitness. Yet this small focus is apparently sufficient to seed the whole of the station with tuberculosis. There are also mission stations to be considered. These are scattered throughout the highlands, and before the last war it was found that there were about a thousand coastal natives engaged in mission work in

TABLE III.
Incidence of Positive Mantoux Reactions in the Central Highlands.

Area.	Group.	Total.	Percentage of Positive Reactions.
Goroka	Station natives.	653	10·4
Goroka	Coastal contacts.	25	56·0
Goroka	Village natives (near).	503	0·7
Goroka	Village natives (distant).	1546	0·24
Mount Hagen ..	Station natives.	448	7·1
Mount Hagen ..	Coastal contacts.	14	7·0
Mount Hagen ..	Village natives (near).	291	0·34
Chimbu	Station natives.	322	14·9
Chimbu	Coastal contacts.	14	20·0
Chimbu	Village natives (near).	1842	0·21
Kainantu ..	Station natives.	193	11·9
Kainantu ..	Village natives (near).	390	2·8

the highlands. The spread of tuberculosis from these foci is likely to be rapid, because of the fact that the natives frequently travel long distances through the highlands. Their housing in small round or oval huts, half sunk in the ground, with a single small doorway and sheltering a large number of persons and pigs, will also encourage the spread.

Trobriand Islands Survey.—The "Mantoux-positive" figures for all the main islands and villages in the Trobriand group are shown in Tables IV and V. The incidence is high. It is surprising to find that almost 70% of the population over the age of thirty years react to 0·1 millilitre of old tuberculin. Frank ulcero-glandular tuberculosis was found, as well as pulmonary tuberculosis.

Port Moresby Area Survey.—The results in age groups in the Port Moresby area are shown in Table VI. Out of 304 natives in Tatana village there were 213 positive reactors. Primary tuberculosis and typical fibro-caseous disease are commonly found in this area. The position is rightly regarded as most serious.

Other Areas.—Two other areas were examined by the use of a number of natives from labour lines from these

TABLE IV.
Incidence of Positive Mantoux Reactions in the Trobriand Islands.

Village.	Number of Mantoux Tests.	Percentage of Positive Results.
Davagila area ..	740	31·8
Kitava Island ..	836	52·8
Vakuta Island ..	328	55·7

areas. This survey gives results only for this age group; but as these natives are picked for their good physique and health the result is certain to be an under-estimate. Among 31 natives from Kikori and 35 natives from Higaturu the "Mantoux-positive" rates were 30·6% and 20·6% respectively. These are coastal and subcoastal areas respectively.

TABLE V.
Distribution of Mantoux Positivity by Age Groups in the Trobriand Islands.

Area.	Age Group. (Years.)				
	0 to 1.	1 to 5.	6 to 12.	13 to 30.	31 and Over.
Kitava Island[1]	—	5·7%	27·2%	50·9%	84·2%
Davagila, Vakuta, Sinaketa ..	13·3%	7·5%	22·2%	44·4%	69·8%

[1] Kitava Island is isolated by one day's canoe journey from the rest of the group.

It is certain that tuberculosis is only too common in coastal areas. It is spreading through the subcoastal areas to the heavily populated inland areas of the central highlands. As has already been stated, the object of the areas are likely to be the centres of large developmental schemes in the near future, and native labour is also being sent from the highlands to infected coastal areas. The

TABLE VI.
Distribution of Positive Mantoux Reactors According to Age Groups in Village Natives in Port Moresby Area.

Age Group (Years) and Number of Subjects.				
0 to 1. (20)	1 to 5. (58)	6 to 15. (71)	16 to 30. (80)	31 and Over. (75)
No reactors.	23 reactors.	47 reactors.	68 reactors.	75 reactors.

problem in the sparsely seeded areas is quite different from that in the coastal belt.

B.C.G. Inoculation Organization in Central Highlands.

It has been found most useful in this organization to work through the administrative areas, as these have present campaign is to check this spread, as many of the already been subjected to census and instructed in the method of congregating at specific points and in specific groups. An area is warned that those living in it are to

be injected two days before this is done, to allow all travellers to be recalled. The response to the request is most satisfactory. The absentee rate is almost always less than 4% to 5%, but there are exceptions. The measures adopted to ensure accurate records have been already outlined. (See above, "Materials and Methods".) So far, over 50,000 natives have been vaccinated.

Mantoux Conversion Rates.

Many thousands of post-vaccination Mantoux tests have been carried out, but only 6000 are reported in detail. The results are from varying batches of vaccine and are presented in Table VII.

TABLE VII.

Mantoux Conversion Rates after B.C.G. Vaccination in the Central Highlands.

Area.	Number of Subjects.	Conversion Rate.
Miruma[1]	1007	98·2%
Koreipa	540	97·5%
Runumbe	1200	99·2%
Asaro	1180	98·1%
Notofana	1073	98·0%
All station natives in Central Highlands	1000	97·7%

[1] All the villages are in the Goroka area.

The distribution of positive Mantoux reactors in grades of severity of reaction and in age groups is shown in Table VIII.

There is seen to be a larger number of strong reactions from birth to the age of fifteen years, and the highest proportion of all is in the one to five years age group. No difficulty has been found in achieving Mantoux conversion in the first year of life. Mild reactions are more common in the higher age groups. The reactions in the aged are particularly difficult to read.

TABLE VIII.

Distribution of Mantoux Positive Reactions According to Grades of Severity and Age Groups.

Reaction.	0 to 1 Years.	1 to 5 Years.	6 to 15 Years.	16 to 30 Years.	31 to 45 Years.	46 Years and Over.
	%	%	%	%	%	%
+	28·6	9·5	24·0	47·1	49·2	68·9
++	57·4	71·4	69·4	47·5	47·1	30·0
+++	14·0	19·1	5·3	5·4	3·7	1·1
++++ ..	0·0	0·0	1·3	0·0	0·0	0·0

Thirty-two pregnant women were in this series, and there was no difference in their Mantoux conversions. Inoculations had no apparent effect on the child. Sixty-three cases of frank secondary yaws were investigated, and there was no significant difference in the results.

Twenty-four lepers (both neural and lepromatous types) in the Native Hospital at Chimbu were Mantoux-tested. Twenty-three failed to react and were vaccinated. All were converted to Mantoux-positive status.

Comparison of Mantoux Conversion Rates with Different Strengths of Old Tuberculin.

Approximately 1000 consecutive subjects were simultaneously tested with 1 in 100 and 1 in 1000 old tuberculin eight weeks after vaccination. The results are presented in Table IX. The only difference noted was in the increased severity of the reactions associated with the larger dose. There seems to be no advantage in using the 1 in 100 dilution for judging the conversion rate, but it may prove useful in later tests when allergy is waning.

Local Lesions following B.C.G. Vaccination.

Six thousand village natives and 330 mission natives were examined at the eighth week and the results are recorded in Table X.

The small ulcero-papular reaction is by far the commonest lesion. Only very few of those with ulceration have required admission to hospital. There have been only three cases of adenitis in this series, and in two of these the lesions discharged and produced sinuses requiring hospital treatment. The incidence of ulcerative lesions from the eighth week and even up to the twelfth week is higher than usually reported. This is almost certainly due to the local conditions. The soil is a rich dark loam which adheres readily to the skin. The natives of this area never wash and apply thick layers of pig grease to all exposed parts. It is not surprising that a small ulceration of the skin persists. Secondary infection occurs rapidly. Also

TABLE IX.

Comparison of Mantoux Reactions following B.C.G. Vaccination with Different Dilutions of Old Tuberculin in 1000 Consecutive Cases.

Dilution.	Reaction.				No Reaction.
	+	++	+++	++++	
	%	%	%	%	%
1 : 100	9·0	19·1	60·1	9·0	2·1
1 : 1000	46·1	46·5	5·4	0·0	2·1

the natives are prone to scratch any swelling of the skin to see what goes on inside. A comparison of village natives with mission natives, who are forced to wash regularly and keep themselves clean, shows the part played by filth. All local reactions in the mission natives are healed by the twelfth week and the vast majority by the eighth week.

Effect of Transport Delays on the Activity of B.C.G. Vaccine.

The effect of transport delays on the viability of B.C.G. is clearly shown in Table XI. Clinical assay in Melbourne

TABLE X.

Local Reactions in Village Natives (6000) and Mission Natives (330).

Reactions.	Percentage.	
	Village Natives.	Mission Natives.
Papules only	30	53
Small ulcero-papular lesions	50	46
Ulcers under 10 millimetres in diameter ..	16	1
Ulcers over 10 millimetres in diameter ..	3·9	Nil
Adenitis	0·06	Nil
Sinus formation	0·04	Nil

of batches 88 and 94 revealed no difference in potency as compared with that of the other lots used.

The results with fresh vaccine are satisfactory, but delay without refrigeration causes a rapid loss of antigenicity. It must be remembered that the vaccine is being transported through tropical conditions. Attempts to increase the effectiveness of delayed vaccine by doubling the dosage have shown that this has little effect in increasing the Mantoux conversion rate. It is noticeable that the delayed vaccine produces almost the same local lesions as does the fresh vaccine. It is useless to rely on the local reaction as an indication of the state of allergy present.

It is evident that to ensure satisfactory results transport time from the laboratory to the field of operations is a crucial factor, unless continuous refrigeration during transit can be provided. There is seldom delay in the field, but unforeseen weather conditions are always likely to upset supply by air. The vaccine on its receipt is stored in a refrigerator, and it is from this centre that the vaccine is distributed by runner, carefully protected from the strong sunlight of the central highlands.

Trial of Freeze-Dried B.C.G. Vaccine.

About 2000 natives were inoculated with a freeze-dried vaccine, prepared some months previously by the method described by Rosenthal (1948). The Mantoux conversion

rate was poor. Even with a dosage containing 0·2 milligramme of B.C.G. the Mantoux conversion rate was less than 50%. The fresh liquid vaccine that gave a 98% and even 99% conversion rate contained only 0·05 milligramme of B.C.G. per dose.

TABLE XI.

Effect of Transport Delays on the Activity of B.C.G. Vaccine.[1]

Batch Number.	Delay.	Mantoux Conversion Rate.
86	No delay.	98·4%
88	Two days' delay.	46·3%
90	No delay.	98·1%
92	No delay.	97·6%
94	Delayed two days in the field.	68·4%
95	No delay.	98·3%
96	No delay.	99·2%

[1] A recent paper by J. D. Aronson and Patricia Schneider (1950), "The Problem of Standardization of B.C.G. Vaccine", *American Journal of Public Health and The Nation's Health*, Volume XL, page 533, shows how rapidly the viability of B.C.G. is lost when the vaccine is prepared by the conventional method.

CONCLUSION.

It must be stressed that this is merely a preliminary report and that even in this difficult country an accurate follow-up and statistical record are being attempted. There are many problems involved, but we believe they can be solved.

ACKNOWLEDGEMENTS.

We are indebted to Dr. John Gunther, Director of Public Health, Papua and New Guinea, not only for permission to publish this report, but for his foresight and enthusiasm which enabled the work to be undertaken. We are also grateful to Dr. F. G. Morgan, Director of the Commonwealth Serum Laboratories, for allowing one of us (E.A.N.) to visit New Guinea at Dr. Gunther's request, both to gain first-hand information on the local conditions and to take some part in the preliminary studies.

The large-scale immunization campaign, in which 15,000 doses of vaccine are now used each week, is made possible only by the enthusiasm of the hard-working field units under most difficult conditions.

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Reports of Cases.

SQUAMOUS EPITHELIOMA OF THE RENAL PELVIS: A CASE REPORT.

By V. S. HOWARTH,

Gordon Craig Fellow in Urology, The University of Sydney, and Royal Prince Alfred Hospital, Sydney.

"Primary neoplasms of the renal pelvis are rare, forming about 5-10% of the tumours of the kidney." (Hinman, 1935.)

THE occurrence of a squamous epithelioma of the renal pelvis associated with a histologically dissimilar malignant epithelial tumour of the upper part of the ureter and with

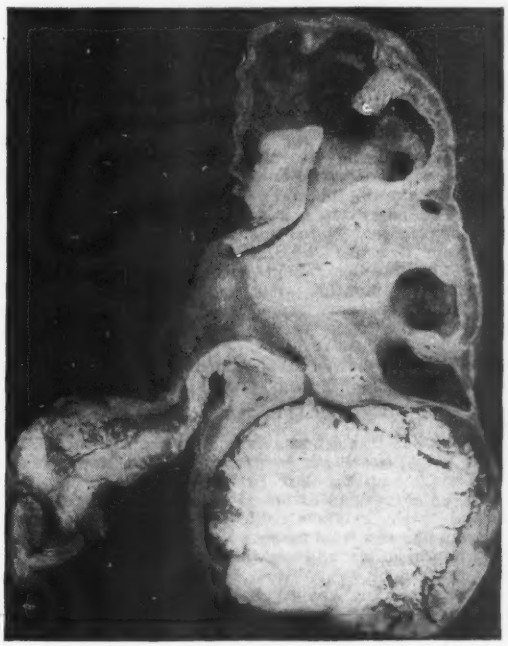

FIGURE I.

The renal substance has been reduced to a mere shell. The renal pelvis is dilated and the lower calyx is occupied by a large tumour measuring 5·5 centimetres in diameter. A nodule of tumour tissue is seen in the upper third of the ureter, quite distinct and separate from the renal neoplasm.

concomitant urinary infection and ureteral calculi is uncommon, and of interest therefore to the clinician and pathologist.

The clinical features of this case and the associated diagnostic problems are illustrated in the following case report.

Clinical Record.

A female patient, aged sixty-five years, had had a severe chill four months prior to examination, and since that occasion had noticed night sweats, loss of weight and nausea. Six weeks before being examined she had first noticed pain in the left side of the back referred to the left costo-vertebral angle and to the left sacro-iliac region, with radiation of the pain down the front of the left thigh. The pain was not severe, but was of a constant aching character. There had been no urinary symptoms apart from nycturia, which had been present for three weeks. She had lost about half a stone in weight over the past four months. Her past history contained no relevant details apart from the fact that she had had "kidney trouble" following a miscarriage twenty-five years earlier.

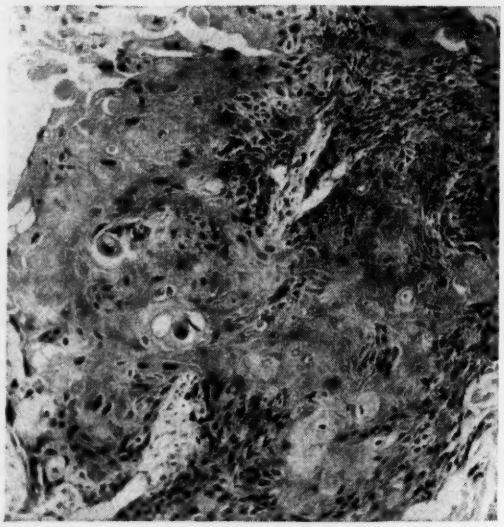

FIGURE II.

A photomicrograph of the histological structure of the renal neoplasm. Magnification 100. The tumour is seen to be a squamous epithelioma with tendency to keratin formation. Many mitotic figures can be seen.

Examination showed the patient to be a frail, thin woman, obviously ill, and with quite apparent loss of flesh. On abdominal examination tenderness in the left hypochondrium and in the left costo-vertebral angle was elicited, but no tumour was detected on palpation. "Heavy" pyuria was present. A cystoscopic examination was carried out, and the left ureter would not permit the passage of a ureteric catheter, which was obstructed just proximal to the ureteric orifice. A clinical diagnosis of a left pyonephrosis was made.

Left nephrectomy and partial ureterectomy were carried out with difficulty. At operation large palpable glands were felt extending along the renal pedicle. The specimen is shown in Figure I, the histological appearances of the renal neoplasm are shown in Figure II and those of the nodule in the wall of the ureter in Figure III.

The patient perished approximately two months after operation.

Discussion.

The histological dissimilarity of the two tumour masses raises the question whether they are independent primary neoplasms arising in a mucous membrane suitably prepared and responding to an extrinsic carcinogenic influence, or whether the ureteric nodule is a secondary anaplastic deposit derived from the pelvic neoplasm. The well-known propensity of epithelial tumours of the renal pelvis to propagate throughout the urinary passages renders the latter possibility most likely, although the former cannot be entirely excluded.

It is apparent that an accurate clinical diagnosis is unlikely to be made in cases of this nature owing to the concomitant pathological states present; but it should be noted that stone is associated with 25% of cases of squamous-cell carcinoma of the renal pelvis.

FIGURE III.

A photomicrograph of the histological structure of the tumour in the ureter. Magnification 100. The tumour is seen to be composed of anaplastic epithelial cells. The structure does not in any way resemble that of the renal neoplasm.

Acknowledgements.

I am indebted to Dr. A. L. Carrodus, of the Department of Urology, Royal Prince Alfred Hospital, Sydney, for permission to publish this case record, and to the Department of Medical Artistry, the University of Sydney, for the photography.

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Reviews.

PYE'S SURGICAL HANDICRAFT.

THE appearance of the sixteenth edition of the remarkable book known as "Pye's Surgical Handicraft" indicates its continued popularity throughout the English-speaking world.[1] Its increasing use in the United States has been recognized by the addition of two American contributors to the team of writers.

In general this book deserves nothing but praise. Intended primarily as a handbook for the house surgeon, it gives him precise details as to how he should conduct every aspect of his work, even including the interviewing of relatives, and his associations with his surgical chief. Everywhere the practical approach is stressed. "House-surgeons have been divided into two classes—those who stand at the foot of the bed, and prescribe, and those who take off their coats, and wash out the bladder. I have found that the ones who take off their coats are more likely to adopt, and succeed in, the practice of surgery."

[1] "Pye's Surgical Handicraft: A Manual of Surgical Manipulations, Minor Surgery, and other Matters Connected with the Work of Surgical Dressers, House Surgeons and Practitioners", edited by Hamilton Bailey, F.R.C.S. (England); Sixth Edition; 1950. Bristol: John Wright and Sons, Limited. 8½" x 6", pp. 730, with 830 illustrations. Price: 25s.

Efficient methods of carrying out all those technical procedures which demand taking off the coat are then described, and usually illustrated with diagrams or photographs. In some chapters, such as that on fractures, the result becomes a complete monograph on the handling of bone injuries.

It is inevitable that amongst so much detail, some statements should be open to criticism. What Mr. Bailey calls "George Ryerson Fowler's priceless gift to abdominal surgery" seems to be advocated with too much fervour, and the alleged advantages of the semi-sitting position are magnified, while the risks of the resultant immobility are minimized. The value of bronchoscopy in the treatment of post-operative atelectasis, though mentioned, is damned with faint praise, the patient being regarded as in no fit state for such a procedure. In the chapter on gastro-intestinal intubation, some statement of the fluid and electrolyte requirements of the patient with acute intestinal obstruction would have been useful. The occurrence of hepatitis, as a complication of the use of pooled human serum, seems to have been omitted. A warning as to the risk of the use of talc powder in sterile gloves during surgical operations might not be amiss.

But these are minor omissions in a book which succeeds magnificently in its stated purpose. Every practitioner of the surgical arts, from the most junior house surgeon to the senior visiting surgeon, needs this book beside him, and none of them could fail to learn much from its pages.

PARAPHILIC PORTRAITS.

THERE is always fascination in scanning a rogue's gallery; and when, as in "Sexual Deviations", two well-known American psychiatrists, Louis S. London and Frank S. Caprio, furnish an entire exhibition with detailed paraphilic portraits, the interest extends to all who are concerned with human behaviour.[1] Here, in this book, are perverts in plenty, frotteurs, sadists, exhibitionists and a host of minor sex variants, tabulated, interrogated, analysed and set out in all the fullness of a psychiatric anamnesis. The reader is led through that half-world of psychosexual infantilism where men and women, suffering from the sexual traumata of childhood, act out their morbid compulsions and aching inferiorities in the hired privacy of faded bedrooms, low-class brothels and public lavatories, in quiet sidewalks and unfrequented subways and in the shuttered sanctity of suburban villas. Many sexual deviates come to grief in the police courts, where they are completely misunderstood, and ordered to serve their futile sentences in gaol. Others bring their paraphilic problems to the psychiatric clinics; and others lead an apparently blameless life, covering up their emotional foibles or sharing them with a long-suffering and timid partner.

Sexual deviations have been presented before. Within the last hundred years Krafft-Ebing, Magnus Hirschfeld, Albert Moll, Havelock Ellis and others have enriched the literature of *psychopathia sexualis* with fresh case material. This has, however, been at the descriptive level; and only since Freudian teaching has spread have the sexologists sought to discover the psychodynamics underlying sexual deviation. The work under review has this special merit. It goes a stage further than the descriptive text-books of a decade or so ago. It seeks to present a psychological understanding and succeeds in establishing the proper significance of sexual deviations. It is clearly written, explanatory, comprehensive and well documented. It presents well-defined cases, ably summarized in the language of the psychoanalyst; and thereby provides the reader with an explanation of conduct which hitherto has seemed merely vicious or utterly irresponsible.

London and Caprio have rendered a service to that branch of medical jurisprudence which embraces sexual deviation. They have shown that no person is born deviated; but that the conduct of adulthood is often trammelled in the past: that the pervert, the exhibitionist, the sadist and the fetishist gratify their sexual desires through the erotic cravings of childhood. They cannot gratify them in any other way because their sexual development has been arrested at a childish level by circumstances over which they had no control. Socially and sexually handicapped, many deviates seek help from the deceptive stimulation of alcohol which decreases inhibitions and brings the infantile sexual behaviour to the surface, and often the offender into the hands of the police. Only the wider dissemination of this knowledge will prevent the present injustice and ultimately benefit society and the individual.

[1] "Sexual Deviations", by Louis S. London, M.D., and Frank S. Caprio, M.D., with a foreword by Nolan D. C. Lewis, M.D.; 1950. Washington: The Linacre Press, Incorporated. 8¼" × 5½", pp. 724. Price: $10.00.

OBSTETRICS AND DIAGNOSTIC GYNÆCOLOGY.

"HANDBOOK OF OBSTETRICS AND DIAGNOSTIC GYNÆCOLOGY", by Leo Doyle, is neither a text-book nor a reference book, but one which presents its material in the most concise form possible.[1] The greater part of this volume is devoted to obstetrics, only about one-sixth comprising chapters on such subjects as the disorders of menstruation, leucorrhœa, pelvic infections, pelvic masses, infertility and endometriosis. The book is essentially for the general practitioner, and makes readily available a practical answer to many of the daily diagnostic and therapeutic problems.

Probably the best chapter is that on the emotional aspects of pregnancy, which includes an analysis of the psychodynamics and outlines the emotional changes likely to occur from the first trimester through labour to the post-partum period. It contains much sound practical advice. The minor symptoms of pregnancy are fully discussed with practical suggestions for their alleviation. The principles governing the relief of pain in labour are clearly defined, with an emphasis on the necessity to individualize treatment. In an adequate review of the analgesics, inhalational and regional anæsthetics in common use, a good word is said for chloroform. The chapters on toxæmias and Rh incompatibility are also well done.

Of adverse criticism there is a little. But half a page is devoted to puerperal infection, and excepting asphyxia, no reference is made to the newborn child. Apart from several minor inaccuracies of fact, it is felt that some of the teaching is wrong. The old warning about the danger of cord traction in the third stage gets its traditional mention, and in italics, too, but no reasons against this practice are proffered. Similarly the so-called Credé's manœuvre, regarded by many as an obsolete procedure, is advocated for "retained, separable placentas". In the treatment of incomplete abortion and placental polypus, the use of sponge-holding forceps or finger is advocated as adequate, the generally used sharp curette being considered dangerous. In septic abortion surgical intervention is represented as never indicated except in life-endangering hæmorrhage—a degree of conservatism fast falling into oblivion. Few would regard as safe the conservation of the ovaries, because they appeared uninvolved, in operation for chorion-epithelioma.

This little book is undoubtedly worth reading, but one cannot strongly recommend the expenditure of dollars for its purchase.

DIPHTHERIA PROPHYLAXIS.

"DEVELOPMENTS IN DIPHTHERIA PROPHYLAXIS", by Lewis B. Holt, M.Sc., of the Wright-Fleming Institute of Microbiology, St. Mary's Hospital, London, is largely a record of the author's researches into the factors governing the variability in potency of alum-precipitated toxoid (A.P.T.) and into the development of his new and improved diphtheria prophylactic, purified toxoid adsorbed to aluminium phosphate (P.T.A.P.).[2]

The variability in the potency of different samples of A.P.T. containing the same amount of antigen even when prepared by identical methods had, as Holt states, "constituted a source of deep concern to the Government, physicians and manufacturers alike". Holt's studies, which began in 1940, have thrown much light on the factors causing this variability. He claims to have shown that it is possible to prepare a potent diphtheria prophylactic of exactly known composition using a suspension of pure aluminium phosphate and a solution of purified toxoid. His work has already been confirmed in Australia and may be said to constitute a further landmark in the prophylaxis of diphtheria—and possibly of other infections. The great advantage of Holt's P.T.A.P. over A.P.T. appears to lie in the ease with which the amount of inert mineral carrier can

[1] "Handbook of Obstetrics and Diagnostic Gynecology", by Leo Doyle, M.S., M.D.; 1950. Palo Alto: University Medical Publishers. 7" × 4", pp. 254, with 45 illustrations. Price: $2.00.

[2] "Developments in Diphtheria Prophylaxis", by Lewis B. Holt, M.Sc.; 1950. London: William Heinemann (Medical Books), Limited. 9" × 7½", pp. 198, with illustrations. Price: 42s.

be accurately controlled. In addition to being a more uniformly potent antigen than is A.P.T., it is, on account of its purity, much less likely to give rise to severe reactions in sensitive persons.

There are two short sections on clinical studies with P.T.A.P. contributed by Dr. Guy Bousfield. The permanence of the immunity fifteen months after one inoculation of 0·5 millilitre administered intramuscularly was such a marked feature that Bousfield thinks we are "well in sight of a single-injection prophylactic against diphtheria". The rest of the book, however, is so technical that it will appeal only to a small group of laboratory workers engaged in similar activities.

Some of Holt's findings fail to support Glenny's depot theory to account for the enhanced potency of precipitated toxoid over its parent liquid formol-toxoid. Holt suggests that this enhanced potency is due to the antigen being efficiently distributed to a larger number of antibody-forming cells rather than to the delayed absorption of the antigen resulting in a secondary stimulus as postulated by Glenny. We believe, however, that this matter cannot yet be regarded as determined.

ASTHMA AND GOLD THERAPY.

"THE MODERN TREATMENT OF ASTHMA WITH SPECIAL REFERENCE TO GOLD THERAPY", by L. Banszky, is, as the title implies, largely devoted to extolling the virtues of aurotherapy; but apart from lengthy details concerning the dosage of gold salts and instructions for treating the complications resulting from their use, there is little new or original work discussed.[1] A series of 203 patients is analysed in which the results of treatment are graded from "very good" down to "no improvement", but inadequate details are given to enable an accurate assessment of the results to be made. The author stresses the importance of "latent tuberculosis" and its relation to asthma, latent tuberculosis being taken to mean anything from familial contact to a pleuritic scar in a skiagram. With regards to the allergic theories and desensitization he states: "For the majority of cases I am certain an attempt at desensitization is only a waste of time and that for the cause of asthma search must be made in quite a different direction."

Just as some schools advocate intranasal surgery and others laud vaccine therapy in the treatment of asthma, so Banszky acclaims gold as the best therapeutic agent, but this book does little to enhance its claims as such, and gold certainly cannot be hailed as the panacea for asthma.

AUTOBIOGRAPHY.

"HAPPY TOIL" is the autobiography of Sir Leonard Rogers, and tells of 55 years devoted to tropical medicine, first in India and later as an administrator in London.[2] It tells a fascinating story of a man's life, and for an octogenarian to title his book "Happy Toil" is adequate indication of the joy which he derived from his chosen sphere of work. He had experience of all aspects of tropical medicine, and these are discussed from clinical, pathological and epidemiological viewpoints. While he regrets his impotence against tuberculosis, his achievements in other directions prove what great advances have been made in the tropics in the past fifty years. Of later years Sir Leonard Rogers has taken an active part in the campaign against anti-vivisectionists, and he published "The Truth about Vivisection".

As Sir John Megaw writes in his foreword: "Sir Leonard's record of achievements is likely to be suspected of exaggeration by those who are not familiar with his work", but the reader can gain some idea of this extent by reading the two appendices which list the author's publications and also the honours bestowed upon him.

This book is an important chapter in the story of the achievements of British medicine in India and makes very interesting reading for medical men and laymen alike.

[1] "The Modern Treatment of Asthma with Special Reference to Gold Therapy", by L. Banszky, M.D. (Berlin), L.M.S.S.A. (London); 1950. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall, Limited. 7" × 5", pp. 140. Price: 10s. 6d.

[2] "Happy Toil: Fifty-five Years of Tropical Medicine", by Major-General Sir Leonard Rogers, K.C.S.I., Kt., C.I.E., LL.D. (Glasgow and St. Andrews), M.D., F.R.C.P., F.R.C.S. (England), F.R.S., Indian Medical Service (Ret.), with a foreword by Major-General Sir John W. D. Megaw, K.C.I.E.; 1950. London: Frederick Muller, Limited. 8½" × 5¾", pp. 294, with illustrations. Price: 18s.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Diagnosis and Treatment of Tumours of the Head and Neck (Not Including the Central Nervous System)", by G. E. Ward, M.D., D.Sc., F.A.C.S., and J. W. Hendrick, M.D., M.S.; 1950. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 10" × 6½", pp. 852, with many illustrations, some of them coloured. Price: £8 1s. 9d.

Intended for the clinician whether he is specialist or general practitioner.

"The Mammals of Victoria: and the Dental Characteristics of Monotremes and Australian Marsupials", by C. W. Brazenor; 1950. Melbourne: Brown, Prior, Anderson Proprietary, Limited. 8½" × 5½", pp. 130, with illustrations. Price: 7s. 6d.

A handbook issued by the National Museum of Victoria.

"The Antihistamines: Their Clinical Application", by S. M. Feinberg, M.D., S. Malkiel, Ph.D., M.D., and A. R. Feinberg, M.D.; 1950. Chicago: The Year Book Publishers, Incorporated. 7" × 4½", pp. 300. Price: $4.00.

The book is "primarily clinical" and is "intended for every physician in any field of medicine in which the use of antihistamines might be considered".

"Pneumoconiosis: Beryllium Bauxite Fumes, Compensation", edited by A. J. Vorwald, M.D.; 1950. New York: Paul B. Hoeber, Incorporated. 9¼" × 6", pp. 676, with many illustrations.

The sixth Saranoc Symposium, one of a series instituted by the late Leroy U. Gardner, and dealing with problems resulting from the inhalation of dust.

"Types of Diabetes Mellitus and Their Treatment", by A. R. Colwell, M.D.; 1950. Illinois: Charles C. Thomas—Publisher. Toronto: The Ryerson Press. Oxford: Blackwell Scientific Publications, Limited. 8½" × 5½", pp. 112, with some illustrations. Price: 16s. 6d.

A practical monograph.

"McClung's Handbook of Microscopical Technique: For Workers in Animal and Plant Tissues", by thirty-five authors, edited by Ruth McClung Jones; Third Edition; 1950. New York: Paul B. Hoeber, Incorporated. 9¼" × 6", pp. 820, with 157 illustrations. Price: $12.00.

A practical handbook.

"Practical Biology for Medical and Intermediate Students", by C. J. Wallis, M.A. (Cantab.); Third Edition; 1950. London: William Heinemann (Medical Books), Limited. 8½" × 5", pp. 420, with some illustrations. Price: 21s.

A laboratory manual with sections on microscopical technique, elementary biochemistry, plant biology and animal biology.

"Man is a Microcosm", by J. A. V. Butler; 1950. London: Macmillan and Company, Limited. 7¾" × 5¼", pp. 168, with some illustrations. Price: 10s. 6d.

A broad survey and interpretation of present knowledge of the nature and basis of life, for the general reader as well as the scientist.

"Savill's System of Clinical Medicine: Dealing with the Diagnosis, Prognosis, and Treatment of Disease for Students and Practitioners", edited by E. C. Warner, M.D., F.R.C.P.; Thirteenth Edition; 1950. London: Edward Arnold and Company. 8½" × 5½", pp. 1232, with many illustrations. Price: 35s.

Fully revised since the previous edition of 1944.

"The Results of Radium and X-Ray Therapy in Malignant Disease: Being the Third Statistical Report from the Radium Institute, the Christie Hospital and Holt Radium Institute, Manchester: Years 1940 to 1944 inclusive assessed at 5 years and 1934 to 1938 assessed at 10 years", compiled by Ralston Paterson, Margaret Tod and Marion Russell; 1950. Edinburgh: E. and S. Livingstone, Limited. 9½" × 6", pp. 168. Price: 10s. 6d.

The title is self-explanatory.

The Medical Journal of Australia

SATURDAY, NOVEMBER 25, 1950.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

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Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

A CONSIDERED STATEMENT ON PAS.

THE introduction and early laboratory and clinical investigation of PAS (para-aminosalicylic acid) were referred to in these columns on July 10, 1948. At that stage opinion was naturally cautious, but it was thought that the drug was likely to be "a valuable adjunct to existing therapeutic measures". In its subsequent development the use of PAS has become bound up with the administration of streptomycin. It has become increasingly evident that this is the main role of the drug, rather than that of an independent therapeutic agent. Since 1948 a controlled investigation into the effects of PAS in the treatment of pulmonary tuberculosis has been carried on under the auspices of the Medical Research Council in Great Britain. The inquiry was planned and directed by a joint subcommittee of the Medical Research Council's Streptomycin in Tuberculosis Trials Committee and the British Tuberculosis Association's Research Committee. The chairman of the subcommittee was Dr. Geoffrey Marshall, and the pathologists of the subcommittee met under the chairmanship of Professor R. Cruickshank. The investigation has now been completed and the report published in the *British Medical Journal*.[1] The report warrants mention here because of its importance, but as the great majority of our readers will have the opportunity in a week or two of reading the report in full in the *British Medical Journal*, we need make only brief reference to its contents. A clinical trial in which PAS and streptomycin were used involved 166 patients with acute progressive bilateral pulmonary tuberculosis. Of these 59 were treated with PAS (P group), 54 with streptomycin (S group), and 53 with both streptomycin and PAS (SP group). Allotment was by random selection. PAS was given in the form of the sodium salt, 20 grammes daily. The daily dose of streptomycin was one gramme. Chemotherapy was given for three months, and observation for the trial continued for a further three months. PAS was less effective than streptomycin. In 34% of the P group there was no appreciable radiological change, compared with 6% of the S group. Radiological improvement was seen in 22% of the P group and in 56% of the S group. The difference was greatest in febrile patients. Improvement was somewhat greater in the SP group than in the S group, but the differences are regarded as small. The proportion of patients becoming "bacteriologically negative" was highest in the SP group. The outstanding effect of combined therapy was on emergence of drug resistance. Strains of organisms with a streptomycin resistance ratio of above eight were isolated in 33 of 49 cases of the S group, and in only five of 48 cases of the SP group; in two of these five there was only a single resistant culture. Deterioration in the condition of members of the S group was related to the emergence of streptomycin resistance.

It is stated in the report that it is now possible to adjudge the place of PAS in the chemotherapy of pulmonary tuberculosis, although it must be emphasized that the comparisons in the present trial apply to the results of treatment given for equal short periods—namely, three months for each drug. No comment can be made on the possible effect of more prolonged PAS or combined therapy. Apart from cases in which chemotherapy could have little appreciable effect, PAS given alone has a place in treatment when there is apparently complete streptomycin resistance. The most important conclusion concerns the use of combined therapy. Through its effect on streptomycin resistance PAS is able to prolong the period of effective streptomycin treatment. As used at present, the main object of any chemotherapy in pulmonary tuberculosis is to prepare selected patients for collapse treatment or chest surgery. In appropriate cases combined therapy should be continued until this objective is gained, whether this is a matter of week or months. The gains may be only transitory, but there should be no delay in the use of other measures at the opportune moment. The combination of PAS with streptomycin not only renders effective administration of streptomycin possible for longer periods than previously, but probably permits also of repeated effective courses. The use of chemotherapy thereby becomes justifiable for a wider range of lesions. The report goes on to refer to the discussion on the advisability of giving streptomycin to patients with lesions which may be expected to heal without either collapse treatment or chemotherapy. The main argument against the use of streptomycin alone in such cases has been that the development of drug resistance might prejudice the prognosis, should there be a relapse with more severe disease at a later date. This argument, it is pointed out, is now less valid, and the extension of chemotherapy to early or small lesions is worth investigation. Evaluation of the results, it is admitted, will be extremely difficult. Moreover, the report concludes, it should still be remembered that neither PAS nor streptomycin is without toxicity, and that the emergence of streptomycin resistance is not entirely prevented by combined therapy.

It may be as well at this stage to draw attention to an article by K. H. Heard, and others, from the Repatriation General Hospital, Heidelberg, Victoria, that appeared in this journal in the issue for October 21, 1950. In it attention was drawn to the occurrence of hypokalæmia as a

[1] *British Medical Journal*, November 11, 1950.

complication of PAS therapy when the sodium salt was used—that is, sodium para-aminosalicylate. There is no indication in the Medical Research Council report, either from direct statement or from the mention of toxic symptoms encountered, that this complication has been met, or at any rate appreciated. It is hoped that this will be the subject of further investigation, as the Victorian report indicates that it is likely to be a serious drawback to this type of treatment; although potassium para-aminosalicylate was considered to be safer than the sodium salt, the opinion of Heard and his colleagues was that it was unlikely that the sodium radicle was responsible for the complications. The present position appears to be that PAS used rightly in combination with streptomycin has indeed proved to be a "valuable adjunct to existing therapeutic measures"; but on the negative side its disadvantageous features require further investigation and assessment.

Current Comment.

ADVANCES IN THE FIELD OF CORTISONE AND ACTH.

IT is difficult in this country to keep up with the advances that are being made overseas in the clinical use of ACTH and cortisone, and with the investigations into the nature of their action. It is apparent from the numerous reports in the literature that they are being administered in an extraordinary variety and number of diseases. It may, indeed, be wondered how scientific some of these trials are, and how far all the activities are just the old feverish search for a panacea. It is certainly too early to draw conclusions in most cases. At a conference on the adrenal cortex held just twelve months ago, and sponsored by the Josiah Macy, Junior, Foundation, Robert F. Loeb offered a partial list of the diseases in which either ACTH or cortisone had been administered. There were 11 groups covering a much larger number of individual diseases, and Loeb made the comment that in the vast majority of these diseases a favourable therapeutic effect had been achieved. The most important results seemed to have been obtained among the collagen diseases (rheumatic fever, rheumatoid arthritis, disseminated lupus, periarteritis, dermatomyositis, scleroderma), and the overt allergies (atopic dermatitis, drug sensitization, hay fever, asthma, nasal polypi). Other diseases listed include glomerulonephritis and the nephrotic syndrome; gout; neoplastic diseases, including carcinoma, Hodgkin's disease, chronic myeloid and lymphatic leuchæmia, and acute leuchæmia; specific infectious diseases, including pneumonia (pneumococcal and virus), tuberculosis, poliomyelitis, infectious hepatitis (chronic) and herpes; cirrhosis of the liver; ulcerative colitis; pemphigus; hyperthyreoidism; and a group of central nervous system and muscle diseases including *myasthenia gravis*, amyotrophic lateral sclerosis, muscle dystrophies, multiple sclerosis and psychoses of various types. Even if this list appears almost fantastically wide, it must still be tantalizing to the Australian practitioner so far away from the source of these remarkable new drugs. However, we must for the present be content with learning what we can about them and their actions. For this there are a number of sound sources. Many have been grateful for the excellent lectures on the subject given by Professor Francis Blake, who recently visited this country from the United States, and there is much of value in the literature apart from the innumerable reports of cases, the significance of many of which is difficult to assess. Attention may be drawn to the conference on the adrenal cortex already referred to, the papers and discussions at which have been published in full.[1] The chairman was C. N. H. Long, and papers were contributed by Edward C. Kendall on the relation of chemical structure of adrenal hormones to biological activity, by Gregory Pincus on the regulation of adrenal cortical secretion, by Robert F. Loeb on clinical studies of cortisone and ACTH, by Conrad Bloch on steroid metabolism in the adrenal cortex, and by Elaine P. Rolli on the relation of vitamins to adrenal cortical function. Other men eminent in this field, including Hans Selye, contributed to the discussion. Another useful symposium that has been published was presented at a special meeting of the New York Academy of Medicine in January of this year.[2] Individual papers were devoted to the effects of cortisone and ACTH on rheumatoid arthritis, on rheumatic fever, on disseminated *lupus erythematosus*, on neoplastic disease and on connective tissue, as well as the physiology of the pituitary-adrenal system and the relationship of adrenal cortical activity to immune responses.

It is as well to remember that the first and most important work in this field was that on the rheumatic diseases, originally reported by Philip Hench, of the Mayo Clinic. On this the most up-to-date information is available in a report of a lecture delivered by Hench in England on October 5, 1950.[3] Hench in his lecture spoke of his previous references to the potential reversibility of rheumatoid arthritis; this had been realized by cortisone. With it pronounced relief of symptoms within a few days had been obtained in 95% of cases. Maximum subjective improvement occurred in up to eight days, maximum objective improvement in up to three weeks, and maximum over-all remission of the disease in all its clinical and biochemical aspects in two to three months. Hench described the striking result, now well known at least by report, obtained with a course of cortisone in rheumatoid arthritis. He said that even contractures of two to three years' standing had completely gone, and physiotherapy might complete a partial cure. The responses to second, third and fourth courses of cortisone were essentially similar. When treatment was discontinued symptoms returned in two to four weeks, but not in all cases. The following over-all results had been obtained: disappearance of over 90% of symptoms in 60% of cases, and disappearance of 75% to 90% of symptoms in the rest, except in a very few severe cases, in which there was only moderate improvement. There was a parallel reversal of laboratory findings. Serial biopsy examination of synovial membrane showed improvement, but in no case of rheumatoid arthritis so far studied had there been a complete reversal of the histological picture to normal. Rheumatic fever and rheumatic carditis presented a different problem. Hench said that one could imagine hypotheses in which the susceptible rheumatic subject, sensitized by unknown inherited or environmental factors, developed what might be called the "latent rheumatic state". The latent rheumatic state, *plus* the presence in the body of the unknown irritant produced by the hæmolytic streptococcal infection of the throat, reacted to give the clinical attack of rheumatic fever. That reaction was in two parts. The first part was exudative, with inflammation, œdema, effusions into synovial cavities and fever, and was relatively unimportant. The second was proliferative, with cellular infiltration, and later fibrous-tissue formation in the sites of rheumatic nodules and in the connective tissue of the heart and its valves. Unless cortisone could suppress that proliferative reaction as well as the exudative, it was of no more use than aspirin. That it could do so was not proved but probable, for the following reasons. Firstly, the granulation tissue of rheumatic carditis was similar to that producible in animals experimentally and to that of rheumatoid arthritis, both of which were known to be suppressed by cortisone. Secondly, certain significant cardiac murmurs had been reported to

[1] "Adrenal Cortex: Transactions of the First Conference, November 21-22, 1949", edited by Elaine P. Ralli; Associate Editors, Konrad Bloch and Gregory Pincus; 1950. New York: Josiah Macy, Junior, Foundation. 9" × 6", pp. 190, with illustrations. Price: $2.00.

[2] *Bulletin of the New York Academy of Medicine*, April, 1950.

[3] *The Lancet*, October 21, 1950.

have disappeared under treatment. Thirdly, in the short follow-up studies so far available, new murmurs indicating fresh carditis had not appeared, and there had been no significant change in established murmurs. Hench insisted that a much longer follow-up time—two to three years—had to elapse before judgement could finally be made. He went on to say that there were good reasons for believing that the average duration of the latent rheumatic state was between six and twelve weeks. Under the influence of ACTH or cortisone, the latent rheumatic state and the unknown irritant were present, though the patient was symptomless for six to twelve weeks. If those hormones were given until the end of the period of the latent rheumatic state, no withdrawal relapse occurred. If the hormones were withdrawn before then, a relapse would occur which would last until the natural end of the latent rheumatic state. It must again be emphasized that rheumatic fever was not "cured", the duration of the latent rheumatic state was not shortened, and subsequent recurrences were not prevented by cortisone. The hope for the future lay in the administration of cortisone to suppress the body's reaction during the latent rheumatic state, and in the oral penicillin chemoprophylaxis of streptococcal infections in susceptible subjects.

Speaking of other forms of arthritis treated, Hench said that of patients with osteoarthritis 50% had shown satisfactory responses. Symptoms of acute gouty arthritis were rapidly suppressed, although relapse might occur on withdrawal of the drug. In chronic gouty arthritis little structural change was seen, despite symptomatic improvement. In tuberculous arthritis symptomatic relief was obtained, but signs of active tuberculosis could still be found, and a culture of organisms could be obtained from biopsy material from the affected joint. Referring to undesirable side effects, Hench said that they were more common in women, especially at the menopausal or adolescent stage, and were mostly associated with long-continued treatment for chronic disease. The incidence had decreased with the lowering of the standard maintenance dosage. Few side effects presented an emergency, but occasionally they demanded special attention and could be dangerous. Search was going on for a drug cheaper, safer and more easily available than cortisone, and over 50 closely related steroids and many adrenal extracts had been tried, but none except compound F had been found to possess antirheumatic activity in the hands of Hench and his colleagues or in the hands of critical rheumatologists experienced with cortisone. A good deal had been learnt about the chemical features on which the antirheumatic properties of a drug depended. However, in the absence of an effective substitute for cortisone it was necessary to learn to obtain the maximum desirable with the fewest unwanted effects. Some preliminary successes had been obtained in that direction. In this it was important to learn to cooperate with, rather than to dominate or supplant, the functions of the pituitary-adrenal system.

Hench described various plans for administration of the drug that had been used, and then went on to discuss certain promising new developments under way. Briefly, they were the improved methods of producing cortisone and ACTH; the development of long-acting ACTH and of ACTH peptides; the potentiation of cortisone with insulin; the production of radio-actively labelled cortisone, and its use in research; the development of compound F; and the studies on oral cortisone therapy. In conclusion he pointed out that at the Mayo Clinic the hormones had not yet been used in routine treatment. However, one could not remain academically aloof to the millions of arthritic patients who asked if they could get the hormones as a safe treatment, and if so, how soon. Many investigators believed that the drugs could now be released for practical application in conditions requiring relatively short-term treatment. The price of cortisone had already fallen from 1000 dollars to 50 dollars a gramme, and the drug was available in every large American hospital. In the management of chronic diseases, and especially in rheumatoid arthritis, current investigations might reveal the limits of its usefulness. Much remained to be learnt, but a satisfactory beginning had been made through the correlated efforts of many investigators in many branches of science. Whatever the destiny of these hormones in practical therapy, they demonstrated clearly the reversibility of certain disease processes formerly regarded as relentlessly progressive, and in particular they were powerful tools with which could be investigated many problems of ætiology and treatment in a wide variety of diseases.

These statements of Hench are encouraging and indeed reassuring, the more so because they are conservative. We may well be confident that a major advance has been made in medical knowledge, even if we have not obtained a cure of all ills.

AN AUSTRALIAN CONTRIBUTION TO GENETICAL KNOWLEDGE.

DURING the past six or seven years we have published at regular intervals papers by R. T. Simmons and his colleagues at the Commonwealth Serum Laboratories, in which have been set out genetical data obtained from blood samples collected from members of the local population in various parts of Australia and the adjacent islands. Those of our readers who have appreciated these papers, and indeed also those who have had little personal use for them, will be interested to learn that the valuable work of Simmons and his collaborators, which is still going on, is becoming part of an even wider project which is expected to make a notable contribution to genetical knowledge. We learn from a recent communication by Joseph B. Birdsell[1] that Simmons has been appointed a research associate in the Department of Anthropology and Sociology of the University of California at Los Angeles, and that he and members of the department have undertaken a long-term collaborative project for the genetical survey of the native populations of the Pacific area. A substantial amount of ground has already been covered by Simmons with J. J. Graydon and others, some of the work being done despite the difficulties of wartime, and Birdsell points out that because of this work, today our knowledge of the population genetics of Australasia is more advanced than in other regions of the world. Collaboration between the Australian and American institutions arose from the feeling that the unusual contributions made by Simmons and his team under difficult circumstances might be further facilitated with organizational, analytical and financial assistance, which could be provided from America. Primary data will be published by Simmons and his laboratory and field collaborators. Periodically members of both institutions will collaborate in publishing analytical syntheses of all the available data. The task of the joint programme, Birdsell states, is visualized in terms of identifying those populations critical in providing essential genetical data relative to programmes centring on the dynamic processes of human evolution. Various aspects include the identification of the basic racial populations in the Pacific area, evaluation of the degree of hybridization in tested populations, the estimation of rates of gene flow, the exploration of the process of genetic drift, and ultimately the design of experiments to attempt to determine the influence of natural selection on serological antigens. Preliminary phases will require a random sampling of populations on a broad area basis to establish the major genetical clines in the region. Later investigations will include detailed sampling in terms of groups which approximate effective breeding populations. Research emphasis will change as the basic genetical data increase. The collaborative effort is apparently going ahead without delay. It is difficult to imagine a more satisfying tribute to the work already done by Simmons and his collaborators than this opportunity to extend it in a survey which, as Birdsell states, promises an efficient and inexpensive way for the rapid expansion of knowledge of population genetics and the testing of evolutionary hypotheses.

[1] *Science*, July 7, 1950.

Abstracts from Medical Literature.

OBSTETRICS AND GYNÆCOLOGY.

Endometriosis and Pregnancy.

H. HUDNALL WARE, JUNIOR (*American Journal of Obstetrics and Gynecology*, April, 1950) reviews the literature on endometriosis associated with pregnancy and reports 13 cases from his private practice, in which the diagnosis of external endometriosis was proved by operation either before or during gestation. He states that it is now generally recognized that conservative surgery is the treatment of choice for women with endometriosis during the reproductive period of life, and subsequent pregnancy is possible. Endometriosis is usually considered to be a disease occurring in women over thirty years of age, but is now being reported with increasing frequency in younger women. Although the association of endometriosis and sterility is known, the author has found in a small group of patients that pregnancy often occurred a few months after conservative surgery. In 13 reported cases, pregnancy occurred in 12 patients after conservative surgical treatment for endometriosis, and one patient had endometriosis during pregnancy which was undiagnosed until delivery by Cæsarean section. A total of 15 pregnancies occurred in the 13 patients with external endometriosis, 14 resulting in delivery of normal living babies at or near term and two in early abortion. The author considers that endometriosis is a more frequent disease than is usually reported. Conservative surgery with preservation of the child-bearing function in young women and those without children is recommended. Even after partial resection of both ovaries involved by endometriosis, normal pregnancy followed in three of the thirteen patients. In four patients seven pregnancies had occurred before the endometriosis was recognized, and the author is prompted to question whether pregnancy early in the reproductive period has an inhibitory effect on endometriosis. He is unable to explain the apparent arrest of endometriosis in some patients after an operation in which one ovary or a part of both ovaries was left without the removal of all the implants and involved tissue. The indications for surgical treatment of the 12 patients with endometriosis were usually increasing dysmenorrhœa, pelvic pain associated with a tender cystic mass in either one or both sides of the pelvis, and sometimes a fixed retroverted uterus. The author's results suggest that the prognosis for a successful pregnancy in cases of endometriosis is better in young women than it is for those women over thirty-five years of age.

Intraepithelial Carcinoma of the Cervix Uteri.

LOUISE A. KAUFMANN, W. KENNETH CUYLER AND ROBERT R. ROSS (*Surgery, Gynecology and Obstetrics*, August, 1950) report investigations of genital smears with particular reference to the diagnosis of intraepithelial carcinoma of the uterine cervix. They state that the examination of genital smears is extremely useful in detecting intraepithelial carcinoma of the cervix, but stress the difficulties in this type of examination and consider that the diagnosis of this lesion by the smear method necessitates pathological verification. Certain benign conditions of the cervix show nuclear changes which may be confused with the atypical nuclei of intraepithelial carcinoma. Smears were examined from 10,029 patients, and in 44 cases (0·44%) the pathological diagnosis of intraepithelial carcinoma of the cervix was made. Clinically in four of these cases only were the patients thought to have carcinoma of the cervix, whereas in 26 the patients were thought to have benign cervical lesions only; 75% of the lesions occurred in patients under forty-five years of age. Classification of the 44 positive results showed the following: 25% of smears were of intraepithelial carcinoma of the cervix; 45% were of suspected lesions; 29% were not differentiated cytologically from invasive carcinoma. Six patients were pregnant when the lesion was diagnosed, and two patients have been pregnant again since the lesions were first noted. The study suggests to the authors that the majority of patients who have intraepithelial carcinoma of the cervix do not show clinical signs or symptoms of the lesion. In interpreting this lesion from smears the cytologist inaugurates procedures which may entail serious economic or social problems for the patient. Investigators in this field should be exceedingly well trained and should work in close co-operation with conservative pathologists. The pathological diagnosis of this condition in pregnant patients presents a problem; the authors attempt to distinguish the lesion which may regress during the puerperium from the lesion which will persist as carcinoma *in situ*.

Contractility of the Human Uterus.

H. ALVAREZ AND R. CALDEYRO (*Surgery, Gynecology and Obstetrics*, July, 1950) describe two new methods for the quantitative recording of contractions of the human uterus during pregnancy and labour, and report results in 120 clinically normal cases. They state that previous methods of recording the contractility of the uterus consisted of internal methods of recording from a balloon placed in the lower uterine segment and external methods in which were recorded changes in shape and position of the uterus from the abdomen. The authors' methods are as follows: (i) The pressure exerted on the amniotic fluid during pregnancy and the first and second stages of labour is recorded on a manometer by puncturing the abdominal wall and uterine wall and noting the changes in level of amniotic fluid which passes into a glass tube. (ii) Intraabdominal pressure is recorded by changes in vesical pressure registered by a catheter passing from the bladder to a manometer; the difference between amniotic pressure and abdominal pressure is considered to represent the pressure exerted by uterine contractions. (iii) Placental pressure is recorded during the third stage of labour by inserting a trocar into the umbilical vein of the cord after the child is born and the cord tied. This trocar is connected to a manometer which records the placental pressure on a kymograph. The placental pressure is considered to be the summation of abdominal pressure, pressure exerted by uterine contractions and pressure exerted by the elasticity of the placenta. The authors consider these methods to be simple and exact; physiological contractions are not disturbed, and a standard unit of measure of contractions is used throughout. The authors state that their results suggest that during pregnancy and all three stages of labour the uterus always exhibits rhythmic contractions without any interruptions. During pregnancy there are two kinds of contractions: firstly, rhythmical contractions of low intensity which are not felt by the patient and not felt on abdominal palpation, their frequency varying between 10 and 30 contractions per ten-minute interval; secondly, non-rhythmical contractions of higher intensity which correspond to painless contractions of pregnancy (Braxton Hicks). Their frequency increases as pregnancy advances, but they remain without rhythm until two weeks before the onset of labour. During the first and second stages of labour the uterus undergoes strong rhythmical contractions of an intensity of 25 to 70 centimetres of water; during the third stage of labour the intensity of contractions varies between 35 and 40 centimetres of water. A relationship is noticed between both the intensity and the frequency of contractions during pregnancy, during the two weeks before labour and during the first and second stages of labour. The frequency of contractions varies approximately in inverse ratio to the square root of the intensity. No definite relationship exists between the pain and the intensity of contractions. The authors suggest that the pain associated with a contraction may be due to some associated factor, such as the dilatation of the cervix in the first stage of labour, the distension of the birth canal in the second stage of labour, and the distension of the birth canal by the placenta at the end of the third stage of labour.

Vaginal Hysterectomy.

ROBERT N. RUTHERFORD (*Surgery, Gynecology and Obstetrics*, July, 1950) describes and illustrates a routine teaching technique of vaginal hysterectomy, which has been evolved from a personal series of over 300 operations without a death and with reduced morbidity and hospital stay in comparison with previous transabdominal hysterectomy. He states that evaluation of the pelvic floor structures and their supports is necessary by careful vaginal examination. Supports of the bladder, urethra and uterus are assessed, and the presence of enterocele, rectocele and perineal weakness is noted for appropriate treatment. Essential points in technique include approximation of the essential supports of the uterus, attachment of the pubocervical fascia to this new sling support, obliteration of the cul-de-sac by tying in the utero-sacral ligaments, and attachment of the recto-vaginal fascial supports to this new apex. Steps in the operation which harass the inexperienced operator are the dissection of the bladder from the anterior uterine wall, the opening of the anterior cul-de-sac, sufficient visualization of the operative field, control of the uterus and the correction of enterocele. The posterior colpotomy wound is used as an "exploratory laparotomy" incision to accomplish delivery of the uterus, and the anterior cul-de-sac can be distended and opened over the surgeon's

fingers introduced through the posterior incision. A method of creating the vaginal vault involving use of all the previous supports of the uterus is described, together with a method of suturing the over-stretched cardinal ligaments to the pubo-cervical fascia of the opposite side.

Adenocarcinoma of the Corpus Uteri.

ERLE HENRIKSEN AND THOMAS MURRIETA (*The Western Journal of Surgery, Obstetrics and Gynecology*, July, 1950) present a clinical and pathological analysis of 336 cases of adenocarcinoma of the *corpus uteri*. They state that the disease was more prevalent in the private-type patient, the average age of patients was 56·4 years, and 69% of patients were post-menopausal. The average age at which the menopause occurred in the post-menopausal patients was 46·2 years. Only 67% of patients were parous; they had borne an average of 2·7 children. Myomata were present in 22% of the surgical or autopsy specimens; endometrial polypi occurred in 26% and cervical polypi in 7% of patients. Pyometra was associated with *adenocarcinoma corporis uteri* in 14·2% of cases, and the authors consider that the incidence of spread of disease beyond the uterus is greater than in cases of similar clinical status without pyometra. Frank bleeding or blood-stained discharge is the most common early sign, but 6·5% of patients presented no symptoms ascribable to the disease. Œstrogen therapy has been administered to 47% of patients over varying periods before diagnosis; the authors suggest that the haphazard use of œstrogens in the treatment of abnormal bleeding often delays the correct diagnosis. Vaginal smear cytology is a valuable screening procedure, but the final diagnosis and decisive treatment depend on thorough diagnostic curettage. Histological grading is frequently difficult because of the atypical endometrium seen in post-menopausal patients. Clinical grouping based on the size of the uterus, fixation of the uterus and evidence of parametrial extension is subject to a 25% error when checked on results of surgery or autopsy. The authors advise that an apparently early lesion may have already spread beyond the uterus, and a large bulky uterus may be operable. An autopsy study of 64 cases of adenocarcinoma of the *corpus uteri* showed parametrial involvement in 45·3%, involvement of the primary lymph nodes in 32·8% and involvement of secondary nodes in 35·9%. Distant metastases were most frequently present in the lung or pleura, the liver, ovary, bowel, adrenal gland and various bones. The authors favour treatment by pre-operative irradiation followed by total hysterectomy and bilateral salpingo-oophorectomy after an interval of six to ten weeks.

Hysterography and Hysterosalpingography.

RICHARD H. MARSHAK, CHARLES S. POOLE AND MORRIS A. GOLDBERGER (*Surgery, Gynecology and Obstetrics*, August, 1950) report a study of 2500 cases of hysterography and hysterosalpingography, and discuss results with reference to technique and safety of the procedure. All patients were observed for at least one hour after the investigation; they were interviewed the following day in reference to pain, rise in temperature or bleeding, and pelvic examination was performed a week later. The indications for uterosalpingography in the series were menometrorrhagia, dysmenorrhœa, sterility, fibroid disease of the uterus and post-menopausal bleeding. Contra-indications were pelvic inflammatory disease, intrauterine pregnancy, purulent vaginal discharge and serious constitutional disease. Various contrast media were used and assessed. The authors state that certain undesirable reactions with lipiodol have been reported since its extensive use since 1922. They include the occurrence of emboli, foreign body reaction within the tubes and peritoneal cavity, and pelvic abscess. Most authors agree that pulmonary embolism following lipiodol injection into the uterus is usually due to direct trauma to the endometrium, injection under high pressure, or injection during menstruation or after the cessation of menstruation or when the operation of dilatation and curettage has recently been performed. In the series studied there were no cases of dye passing into the veins and no pulmonary complications. The authors state that when lipiodol is used the volume of fluid injected should not exceed eight millilitres and the pressure should not be taken beyond 200 millimetres of mercury. Fat granuloma in the uterine tubes occurred once in the 2500 cases and was noted at operation eight months after hysterosalpingography. "Skiodan", "Visco-rayopaque" and "Rayopaque" are quickly absorbed, eliminate the risk of embolus formation and cause no foreign body reaction. Their rapid absorption precludes the possibility of a twenty-four-hour X-ray film, which in some cases is necessary to demonstrate tubal permeability. The authors consider that the optimum time for hysterosalpingography is one week after the cessation of the menstrual period. Preliminary bimanual examination and introduction of a uterine sound, and slow and gentle injection of the medium in fractional amounts are stressed in technique. Complications due to the contrast media are pain, peritonitis, endometritis, allergic phenomena and emboli. Pain varied with the volume of medium injected and the different contrast media employed: 80% of patients experienced some degree of pain, but this could be relieved by injection of 50 milligrammes of "Demerol"; lipiodol and "Rayopaque" caused the least pain; 14 patients suffered prolonged pain and showed signs of peritoneal irritation. Four hundred and fifty uteri and tubes were excised and studied at intervals of one day to one week after uterosalpingography; no reaction was noted after the use of "Skiodan Acacia", "Rayopaque", "Hippuran" or "Diodrast". In eight cases after the use of "Visco-rayopaque" the endometrium was swollen and hyperæmic. Nine patients developed urticaria after the use of the water-soluble media. Emboli did not occur in any of the 300 cases in which lipiodol was used. Complications due to the procedure include hæmorrhage, acute exacerbation of chronic pelvic inflammatory disease, perforation of the uterus, shock, entry of dye into the uterine vessels, and introduction of dye into a pregnant uterus. Three patients experienced severe bleeding after hysterosalpingography; one patient had a submucous fibroid tumour, a second had an endometrial polypus, and a third had extensive pelvic endometriosis. An acute exacerbation of chronic pelvic inflammatory disease occurred in seven cases resulting in pelvic peritonitis. Colpotomy was necessary in three of these cases. The uterus was perforated once in the series of cases studied; this was done with the uterine sound, and dye was injected through the perforation into the peritoneal cavity. Mild shock was noted in three cases. Two patients with unsuspected uterine pregnancies had utersosalpingograms for sterility. Circular filling defects were noted in each case, and pregnancy continued uneventfully. Dye entered the uterine vessels in 38 cases, but all the patients concerned had been investigated with water-soluble media and no embolism occurred. The authors conclude that complications due to the contrast media are not serious, nor do they cause any permanent harm to the patient. Complications of the procedure itself are relatively few. The perfect contrast medium has yet to be found, but the water-soluble media are very satisfactory, despite the fact that a twenty-four-hour X-ray film is not possible. There should be no hesitation in the use of the procedure when indicated.

Aureomycin in Obstetrics.

J. A. GUILBEAN *et alii* (*The Journal of the American Medical Association*, June 10, 1950) state that the normal post-partum uterus contains a wide variety of bacteria; an anaerobic streptococcus of various types predominates. Most Gram-positive and Gram-negative organisms isolated by the authors were susceptible to aureomycin *in vitro*; clinical results appeared to correspond. Aureomycin proved effective in various obstetric infections such as peritonitis, endometritis, parametritis, infective abortion and intrapartum infection. Patients with acute and chronic infections of the uterine tract treated during pregnancy responded satisfactorily to therapy, although relapse occurred in several cases when treatment was discontinued. The authors discuss the indications for prophylactic administration of aureomycin during labour and the early puerperium, and analyse their observations in 75 cases. They state that placental and mammary transfer of aureomycin occurs rapidly and in high concentrations. They regard aureomycin as a highly desirable chemotherapeutic agent because it is effective after oral administration, it possesses a wide range of antibacterial activity, and it is unassociated with serious toxic manifestations.

Abortifacient Pastes.

F. R. DUTRA, F. P. CLEVELAND AND H. P. LYLE (*The Journal of the American Medical Association*, July 8, 1950) review the dangers of criminal abortion by the introduction of abortifacient pastes into the uterus and report seven cases of deaths resulting from this practice. They state that the deaths resulted from necrosis of the uterine wall with peritonitis, from diffuse peritonitis without perforation of the uterus, and in two cases from paste embolism; in one of the two last-mentioned cases there was a patent *foramen ovale* which predisposed to paradoxic embolism. There is evidence that the common lethal agent in all abortifacient pastes for intrauterine administration is soap. Experiments are reported which demonstrate the toxicity of soap.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on August 31, 1950, at the Robert H. Todd Assembly Hall, British Medical Association House, 135 Macquarie Street, Sydney, DR. G. C. HALLIDAY, the President, in the chair.

Congenital Malformations.

PROFESSOR LORIMER DODS discussed congenital malformations following rubella and other noxious influences during pregnancy. He said that he was both pleased and frightened to see Dr. Donald Hunter sitting in the front row and said that he was very glad to see Dr. Norman Gregg in the audience, as it was his dramatic incrimination of maternal rubella as a cause of congenital malformations which had opened up that wide and important field of preventive medicine which had been called "pre-natal pædiatrics". The subject of "pre-natal pædiatrics" included the study and the possible control of those noxious influences occurring during pregnancy which might affect the normal development of the infant—influences which might be responsible for a miscarriage or a stillbirth or the much sadder picture of a living and deformed infant. Various estimates had suggested that about 2% of all newborn infants exhibited some form of minor or major congenital malformation, that the incidence of those defects might be as high as 5% to 7% amongst premature infants, and possibly as high as 30% to 40% amongst infants who died before reaching a viable age. Unfortunately those figures did not take into account those congenital malformations which were not obvious until much later in life or were recognized only after death. Professor Dods pointed out that the falling infantile mortality rate of recent decades had led to an increase in the relative significance of congenital malformations as a cause of death during the first year of life; in 1900 congenital malformations were responsible for less than 3% of the infantile mortality in Australia, while during the period 1941-1945 those defects were responsible for about 10% of the infantile mortality and represented the second most common cause of death during the first month of life.

Professor Dods said that for many years it was taught that the majority of congenital malformations were genetically determined, but during the past decade an increasing knowledge of the effect of various noxious influences on the developing fœtus had shaken that dogmatic generalization about so-called "germ plasm defects", and it now seemed reasonable to assume that the normal growth of an ovum depended on (*a*) its genetic constitution, over which the medical profession had no control, except perhaps as eugenists, and (*b*) various maternal and external environmental factors, some of which the medical man might be able to control. Professor Dods reminded his audience that Gregg's original report, which emphasized cataracts, microphthalmia and congenital cardiac defects, appeared in 1941 and was followed by a wide survey of the problem by Swan and others in South Australia, which confirmed Gregg's original conclusions and defined further defects, including deaf-mutism.

Professor Dods drew attention to the fact that Gregg's discovery had focused the attention of the medical world on the first twelve weeks of intrauterine life, those hazardous weeks when extremely rapid cell division was responsible for converting a single cell into a fœtus and for determining the ultimate structure of many important organs. His work also emphasized the great importance of certain "critical periods" in the developmental life of organs and tissues, periods when very rapidly dividing cells were particularly susceptible to disturbance by various noxious influences, and when the chances of repair were minimal. Professor Dods admitted that it was impossible to produce accurate figures about the exact stage of pregnancy at which the mother suffered from rubella, but pointed out that the available evidence supported the conclusion that the nature of the congenital defects bore some relationship to the approximate stage of pregnancy at which the mother developed the disease. A review of 130 Australian case histories suggested that the incidence of cataracts was greatest when the maternal rubella occurred at or about the sixth week of pregnancy, and that the incidence of deafness was greatest when the rubella occurred at or about the ninth week of pregnancy—figures which were consistent with the theoretical concepts of the "critical periods" in the development of the lenticular and cochlear *Anlagen*. Professor Dods went on to define and discuss the various congenital defects which might follow maternal rubella during pregnancy, and pointed out that the congenital cardiac anomalies had usually taken the form of patency of the *ductus arteriosus* or of a septal defect. He was interested to know why maternal rubella was rarely responsible for the cyanotic types of congenital heart disease, which were probably initiated during the fourth to the sixth week of pregnancy, and why this infection occurring during the early months of pregnancy should frequently be associated with failure of closure of the *ductus arteriosus* nearly a year later. The statement that "what heredity can do environment can also do" was illustrated by the fact that patent *ductus arteriosus* might occur initially as a familial disease or might follow maternal rubella.

Professor Dods admitted that it was not known how the maternal rubella produced the fœtal abnormalities. Although it had been suggested that the rubella infection actually occurred in the cells of the embryo, that had not been established, and it was possible that the effect was an indirect rather than a direct one. The simple conception that rubella infection actually reached the fœtus was possibly confused by the suggestion that rubella occurring shortly before conception had been followed by classical congenital deformities. Professor Dods reviewed some of the case reports which had suggested that "pre-conception rubella" might be a cause of congenital defects and concluded that the available evidence was far from complete.

Professor Dods said that after an attack of rubella during her pregnancy, a mother might suffer a miscarriage, might be delivered of a stillborn or living child with deformities, or might give birth to a normal child. It was very difficult to offer any accurate statements about the frequency with which congenital defects following rubella occurred during various stages of pregnancy, and with much hesitation Professor Dods suggested that there was possibly about a 70% chance that rubella occurring during the first three months of pregnancy would be followed by some defect in the infant, and that the incidence of such defects fell sharply after the fourth month, diminished with each month of pregnancy and reached negligible levels during the last trimester. Professor Dods emphasized the fact that the figure of 70% was much higher than that quoted by certain authorities, and that in some of the affected infants the congenital defects might be of a minor nature. He agreed with various authorities, including Burnet, McLorinan and Anderson, that no exact statement about the prognosis for the infant could be offered without a more accurate method of diagnosis of rubella and some carefully controlled wide-scale "prospective" studies of the infants of mothers who had suffered from rubella during their pregnancies.

In discussing the prevention of rubella during the childbearing period, Professor Dods said that an ideal solution of the problem would seem to be a race of young women immune to the disease, and that since an attack of rubella provided a relatively high degree of immunity, it might seem reasonable to suggest that all girls should be exposed to the disease in the hope of achieving an attack before adolescence. Unfortunately uncontrolled and haphazard infections of that type would mean an increased hazard of rubella for such susceptible mothers as were in contact with the children infected, and a more reasonable approach to the problem would be the planned and purposed infection of adolescent girls at an appropriate time by contact with the disease or by the inhalation of atomized throat washings collected from rubella patients at the height of the disease. Burnet and Anderson had induced rubella in a small group of volunteers by means of inhalations of atomized throat washings obtained from patients during the height of the disease, and they had shown that the virus in those throat washings could be preserved in a fully active state for at least three months. Professor Dods considered that rubella convalescent serum or α globulins should be given to any woman who was exposed to the risk of rubella during the first four months of her pregnancy, that those agents should be given as soon as possible after exposure, and that in the administration of such treatment it should be remembered that even the mildest attack of maternal rubella could injure a fœtus and that a sufficient amount of immunizing agent must be given as early as possible after contact in an attempt to prevent the disease. In Victoria, rubella α globulins had been produced by the Walter and Eliza Hall Institute of Medical Research, the Commonwealth Serum Laboratories and the Red Cross Blood Transfusion Service. Dr. H. McLorinan, who had controlled the distribution of rubella α globulins in Victoria, had informed Professor Dods that 540 women exposed to rubella at a vulnerable stage of their pregnancy had been

given two to four millilitres of the product intramuscularly and that there had been a failure to protect in seven instances. McLorinan had concluded that if the product was given soon after contact, there was more than a reasonable chance of preventing rubella.

McLorinan had emphasized the need for further observations of the problem over a longer period and had drawn attention to the following variables: (*a*) all subjects with whom contact was reported might not have been suffering from rubella and the duration and intimacy of contact might have been minimal in some instances; (*b*) some of the patients given a globulins might have suffered clinical or subclinical rubella at an earlier stage of their lives; (*c*) some of the mothers might have suffered subclinical attacks of rubella after receiving the immunizing agent, and a follow-up examination of their infants would obviously be necessary for an exact definition of the situation.

In New South Wales rubella convalescent serum prepared by the Red Cross Blood Transfusion Unit under the direction of Dr. R. J. Walsh was available; a dose of 30 millilitres of the product had been given intravenously to 60 women exposed to infection, and no attacks of rubella had been recognized in the group.

Professor Dods considered that if an attack of rubella was recognized during the first trimester of pregnancy, it was probable that nothing would be gained by the administration of serum or a globulins. A frightening aura of religious, moral, emotional and legal considerations surrounded and possibly confused the attitude towards the question of therapeutic abortion in such cases, but a realistic consideration of the evidence might convince some medical men that an established attack of rubella occurring during the first three months of pregnancy should prompt consideration of the question of termination of pregnancy. Professor Dods hoped that Professor Bruce Mayes would discuss this very difficult problem in some detail.

The recognition of the fact that certain congenital defects followed maternal rubella during pregnancy naturally aroused interest in the possibility that other virus diseases occurring during pregnancy might be responsible for the production of other or similar congenital defects. During the past nine years various malformations, including cardiac defects, eye defects, deafness, hydrocephalus, microcephalus, cleft palate and other developmental anomalies had been observed to follow measles, mumps, varicella, *herpes zoster*, infectious mononucleosis and so-called "influenza" occurring during the earlier months of pregnancy. Professor Dods said that he had been most impressed by the frequency with which congenital anomalies of the central nervous system appeared amongst the children born to mothers who had suffered from *herpes zoster* or mumps during the early stages of their pregnancy, and suggested that it was possible that wider surveys of the infants of mothers who had suffered from those and other virus diseases during pregnancy might establish the fact that such diseases were nearly as significant as rubella in the causation of congenital anomalies.

The possibility that vaccination against smallpox carried out during the early months of pregnancy might affect the embryo had been denied by workers at the Sloane Hospital for Women, New York, who did not find a significant increase in the incidence of congenital malformations amongst the infants of 633 mothers who were vaccinated during the early months of pregnancy in the year 1947.

Professor Dods briefly reviewed a number of other noxious influences occurring during pregnancy which had been associated with congenital defects of the infant. He discussed the importance of the mother's nutrition during pregnancy and mentioned Warkany's animal experiments, which had demonstrated that groups of specific congenital deformities might follow various vitamin deprivations during the pregnancy of a rat. He emphasized the increase in the incidence of congenital malformations amongst infants born to mothers of more than thirty-five or forty years of age, and pointed out that the incidence of congenital defects amongst the infants of mothers of more than forty years of age was three times as great as that amongst the infants of mothers of less than thirty years. He quoted Fraser Roberts's statement that if the average age of the pregnant mother in England could be reduced by five years, the frequency of congenital malformations amongst the children of that country would be halved.

Professor Dods said that he had been impressed by the frequency with which uterine hæmorrhage during the first trimester of pregnancy had been followed by the birth of an infant suffering from some congenital malformation, more particularly digital or cardiac defects. He admitted that it was merely an impression and that further studies would be necessary before it could be confirmed. He pointed out that many authorities had stressed the association between hydramnios and congenital defects; whatever the pathology of hydramnios might be, the association with congenital malformation suggested that the original pathological changes responsible for hydramnios probably occurred during the first twelve weeks of embryological development. Wide-scale "prospective" studies, based on a planned review of all infants born to mothers who had suffered from early uterine hæmorrhages or hydramnios or other evidence of uterine abnormality, might help to establish the significance of those disturbances as causes of congenital malformations.

Murphy, in his text-book "Congenital Malformations", had emphasized the significant increase in congenital malformations amongst infants born after a "prolonged period of infertility", but Dr. Alan Grant, who directed the sterility clinic at the Women's Hospital, Crown Street, had produced figures for Professor Dods which failed to substantiate Murphy's statement.

Professor Dods said that little was known about the effect of sublethal doses of abortifacients on the developing embryo or fœtus, but that it seemed reasonable to assume that those drugs, which were usually taken during the "organo-genetic" period of development, might be responsible for a certain number of congenital malformations. Professor Dods reviewed very briefly the possible part played by therapeutic radium or X-ray treatment of the pelvis during pregnancy, maternal diabetes and toxoplasmosis in the production of congenital malformations. He pointed out that, although genetic factors might possibly explain occasional cases of mongolism, the available evidence suggested that the great majority of mongols were probably the result of multiple and partial "arrests in development" originating at about the seventh to the ninth week of fœtal life, that the nature of the noxious influences responsible for those arrests was not known, but that factors which might play a part in their production included uterine abnormality, maternal infections and the age of the mother.

Professor Dods hoped that his emphasis of noxious influences during pregnancy as possible causes of congenital malformations would not give his audience the impression that he was belittling the significance of the genes in that respect. He was fully aware that some of the malformations might be genetically determined, and that others might be the result of genetic and maternal environmental factors. While he did not want to minimize the importance of the genetic factors, he did want to emphasize the fact that the medical profession might be able to prevent a significant number of congenital malformations by protecting the mother from certain noxious influences during her pregnancy, and that it was their responsibility to find out what those noxious influences were and to do what they could to prevent them. Professor Dods said that, as a first step in that direction, Dr. F. N. Street would be undertaking a long-term and large-scale survey of the problem; Dr. Street would study a wide range of noxious influences during pregnancy, and his study would be both "prospective" and "retrospective" in nature.

PROFESSOR B. T. MAYES discussed fœtal abnormalities and obstetric management. He said that the idea that a noxious influence might affect the fœtus was a very old one. The difference was in the type of noxious influence. It had ranged from the mystical—the witch's spell—to the emotional, and currently, reflecting the more scientific age—the virus. Although the emotional idea had been dropped completely, vaso-vagal effects on the placental circulation were not unlikely; how far, however, those could affect the fœtus, unless severe, prolonged or repeated, was open to considerable doubt. Barton Hirst (Pennsylvania, 1912) held the view that profound impressions upon the mother certainly influenced the psychical development of her offspring and made the interesting statement that "the idiocy of Barnaby Rudge, due to maternal shock and fright, was a fiction founded on fact; that the horror of King James at the sight of a naked sword may well have had its origin in the murder of Rizzio before the eyes of the pregnant Queen Mary". Such an effect, Professor Mayes said, would appear to belong to the realm of speculation. Convincing evidence was lacking that "maternal shock and fright" had a detrimental effect on the offspring. One would think that the horrors of World War II would have provided ample material from which to draw a conclusion.

Professor Mayes went on to say that since the effect of rubella on the fœtus had been demonstrated, it was natural that other viruses should be suspect. Professor Burnet's comment to him some time previously on the question was that if the association of fœtal damage with

rubella was a fact, it should theoretically hold also for other viruses. The question had arisen over two cases of early pregnancy with chickenpox. In both cases the children were born perfectly healthy. It was necessary therefore to try to preserve an elastic mind on the subject while each individual doctor exercised a remorseless precision in the observation of pregnant women. In that, Professor Mayes regarded the general practitioner as the major observer, because he knew the family and personal history so intimately. Professor Mayes therefore suggested the taking of a most careful history as a fruitful source of valuable information on the incidence in pregnant women of such factors as the "flu", tonsillitis, chickenpox, mumps and so on. He assured any keen practitioner that such a careful history, "tied up" with the normality or otherwise of the infant, would provide most valuable evidence on what at the present was expressed mostly as impressions.

Professor Mayes went on to say that he regarded the spontaneous miscarriage as a genetic filter for preserving a reasonable standard of normality. There were many causes of miscarriage, but he was sure that some miscarriages were due to noxious influences. How they acted was another question. It might be through death of the fœtus or by promotion of a contractile state of the uterine muscle.

Referring to conditions of the maternal blood that stimulated the pregnant uterus to contract, Professor Mayes said that it was likely that the toxins of the infectious diseases in the maternal blood might excite active contractions in the pregnant uterus. Whether that was due to some irritative action of the toxins, or to a diminution of the oxygenating power of the blood, as yet remained in doubt. The last-mentioned condition might explain the abortions occurring in pneumonia, as well as in chronic heart disease. It was possible, also, that strong emotions would account for the action of the uterus when women had been terrified. But it was more likely that the action was analogous to that of the rectal and vesical muscles in nervous defæcation and urination. Baudelocque was reported to have said in his lectures that "after the explosion of the powder-mill in Grenelle, he was called to see sixty-two women, either aborting or threatened with abortion". In all maternal diseases accompanied by fever the thermic irritation of the uterine muscle might be responsible for the expulsive efforts of the uterus. It was interesting, however, to note how immune pregnancy was to physical stress in the absence of a toxic factor. Most doctors could recall patients whose experiences had similarity to at least some of the interesting ones described by Hirst in the following statement:

> Some women can make the most violent exertion, can receive the roughest treatment, without bringing pregnancy to an end. English women have followed the hounds in the early months of pregnancy without aborting. Sounds have been introduced into the pregnant uterus; intra-uterine injections have been given; strong applications have been made to the endometrium; trocars have been plunged through the uterine wall; a pregnant woman has been thrown violently from her carriage; another fell from a third-storey window, fracturing her skull and breaking a leg; a young girl, five months pregnant, cast herself from the Pont Neuf into the Seine; in another, fifteen leeches were applied to the cervix of a pregnant uterus; Emmet's operation has been performed upon the cervix during the second month of pregnancy; ovariotomy and other serious surgical operations have been repeatedly performed, the spleen has been ruptured by violence and has been extirpated—all without inducing abortion or premature labour.

Professor Mayes said that he had been asked to speak on the disagreeable subject of termination of pregnancy when it was thought that rubella would have affected the embryo. His view on the matter was his own personal one. If the diagnosis of rubella had been confirmed in the first two months of pregnancy his experience had been that the mother's mental state had become so severe owing to the nightmare of a probably defective child, that termination of pregnancy had been considered justifiable. However, he had always been conscious of the conflict in that, as in others reasons for early termination of pregnancy, and he would like to quote what he had personally written on the matter—a view that he still held:

> **The doctor's opinion on interruption of pregnancy occasionally conflicts with the religious creed of a patient.**
>
> **The medical opinion may favour interruption.**
> **The religious belief of the patient may oppose it.**
> **What to do?**
>
> I have been asked to comment on this difficult position; it is, of course, a personal matter and not a scientific one. I can best adhere to the practical principle by stating what one has personally done in such circumstances.
>
> Firstly, before communicating the medical opinion to the patient and her husband, one has ascertained their religious belief. This knowledge helps one to couch the approach in such a way as to lessen the intensity of any medical and moral conflict.
>
> Secondly, in the case where conflict may arise, having given a medical opinion, one has always told the patient that one is at the same time alert to the moral teaching of a particular church and has given the patient the option of seeking the opinion and care of a doctor of her belief.
>
> The onus is then on the patient; but in the event of her rejecting the original medical advice, I presume that the doctor giving it would be justified in disclaiming responsibility for the result and might consider transferring the patient to another doctor.

Professor Mayes then referred to complications in pregnancy and labour due to fœtal malformations. He said that whatever the cause of those abnormalities, or as the modern embryologist would prefer to call them "mutant characters", the obstetricians had to carry the responsibility of delivering them. Sometimes that meant more than a sympathetic psychological understanding of the distressed mother who had given birth to a monster. It might mean a major difficulty in the physical management of a pregnancy or labour. Such difficulties might be due to hydramnios, hydrocephalus, iniencephalus, fused twins, opisthotonus, anencephalus, and atresia and stenosis of the urethra. (At this stage Professor Mayes showed slides of specimens illustrating the difficulties he had mentioned.)

Commenting on future prospects, Professor Mayes said that the notable observations of Dr. Gregg had opened the avenue to a field in which a scientific approach was being made to the understanding of a very difficult problem in obstetrics. Practically every mother worried at some time or other about the chances of her having a deformed child. At the present time investigators were on the threshold of knowledge of the cause of deformities. With understanding of the cause, it was hoped, would come the really effective approach, which was their prevention.

DR. R. I. FURBER congratulated the speakers on their papers, and said that he wished to express disagreement with one point made by Professor Mayes. Professor Mayes had referred to the case in which he was satisfied that a patient in the first four months of pregnancy had suffered from rubella, and in which he had advised termination of pregnancy; because of the patient's religious beliefs that was refused, and Professor Mayes considered the obstetrician justified in asking the patient to transfer herself to the care of another doctor. Dr. Furber thought that opinion wrong. If two courses of action were possible, the individual patient had the right to choose which course she wished to follow. It was wrong to adopt a dogmatic attitude. Otherwise, with the advice given by both Professor Dods and Professor Mayes, Dr. Furber was strongly in agreement. One point that had not been sufficiently stressed was the great relief afforded by Dr. Norman Gregg's work to mothers who had had children with the abnormalities under discussion. When they asked for advice, it was possible to assure them that such an event would not occur again. Dr. Furber also referred to the great advances to which Dr. Gregg's work had pointed the way, and which had been only foreshadowed by Professor Dods.

DR. R. J. WALSH referred to Professor Dods's remarks about the mechanism of production of the lesions due to rubella—that they might be indirect rather than direct effects of the virus itself. Dr. Walsh said that it had recently been suggested by some Dutch workers that the virus of rubella, by some form of antigen-antibody reaction, might produce a state of auto-immunization. There were a number of analogies in hæmatology. With regard to the prophylactic treatment of the mother exposed to rubella, and the risk of occurrence of homologous serum hepatitis following the use of pooled serum, which had been mentioned by Professor Dods, Dr. Walsh agreed that if serum from a single donor was given the risk was less. On the other hand, if γ globulin was used, as in Melbourne, there was a slightly greater risk of homologous serum hepatitis, but a greater chance of obtaining a consistently good supply of specific antibodies. Passive immunization offered the greatest hope of prophylaxis at the moment, but one should be cautious about accepting it absolutely. The number of cases in the Melbourne series was relatively

small, and there was no control series. No one knew what the natural infection rate was and an investigation to assess the adult attack rate of rubella would be valuable. As to dosage, they were working in the dark. It would seem that the larger the dose, and the earlier after exposure it was given, the better the result. But supply and demand had to be assessed. The serum was relatively hard to obtain; there were few adult rubella convalescents. The figure quoted by Professor Dods, 30 millilitres of serum, represented an attempt to compromise between the largest possible dose and a dose allowing a fair share to be given to all the people exposed to infection. Dr. Walsh again referred to the difficulty in obtaining the serum, and asked for every assistance to be given to those collecting serum for that purpose.

DR. H. O. LANCASTER said that he would like to raise a point of theoretical interest. He asked if epidemics of deafness had occurred before those, reported by Gregg and others, of the years 1938 to 1941, or if the recent ones were unique. Enumeration of the deaf-mutes in the Australian censuses of 1911, 1921 and 1933 had shown that there had

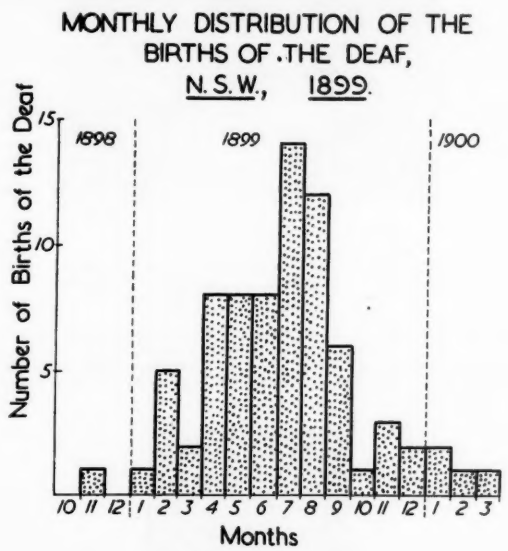
MONTHLY DISTRIBUTION OF THE BIRTHS OF THE DEAF, N.S.W., 1899.
Number of Births of the Deaf
15
10
5
1898
1899
1900
10 11 12 1 2 3 4 5 6 7 8 9 10 11 12 1 2 3
Months

FIGURE I.

been more deaf-mutes born in the years 1896 to 1900 than would have been expected from experience prior to 1896. Dr. Lancaster had followed this clue by obtaining from the Superintendent of the New South Wales Institution of the Deaf and Dumb and the Blind, Darlington, Sydney the dates of birth of all deaf persons admitted for training. There were 15 births recorded for 1898, 70 for 1899 and 16 for 1900. Within the year 1899, there was evidence of an epidemic wave of births of the deaf with a peak in June of that year. Dr. Spencer, of Enmore, and Dr. R. Scot Skirving had both reported epidemics of rubella in the year 1898, and so it appeared possible that many of the cases of deafness in 1899 could be ascribed to rubella, with the reservation that there was also in 1898 a very severe epidemic of morbilli. Dr. Lancaster illustrated the point by means of a graph (Figure I).

DR. H. H. SCHLINK said that the failure to mention one point had surprised him; the influence of viruses and noxious drugs had been mentioned, but not their effect on the ovary, as in mumps. Referring to Professor Mayes's paper, Dr. Schlink recalled two cases of interest on the influence of the ovary in gestation and miscarriage. The first patient was three months pregnant, with destructive pyosalpinx, and both ovaries and Fallopian tubes had to be removed. She carried through to the birth of a baby at seven and a half months. The pregnancy was stormy, and the patient spent a large amount of time under opium. The second patient had one ovary preserved, and it contained a *corpus luteum*; that woman also had a live baby, but on the estimated day of confinement. Dr. Schlink thought that the noxious influences might work through the ovary in congenital malformations and miscarriages.

DR. DONALD HUNTER said that in one week in Sydney he had had the privilege to listen to discourses on three subjects to which Australian workers had made notable contributions—cancer of the skin from actinic light, lead poisoning in Queensland, and the subject under discussion at the meeting. He had had one experience only in that subject, and that was concerned with his work as curator of the museum of the London Hospital Medical College. His head technician, who had been doing museum work for thirty years, asked his advice about his wife, who was unhappy in her first pregnancy. The story suggested that she might have hydramnios, and she was later delivered of an anencephalic fœtus. The technician later came to him in some distress, to ask whether the disaster could have been caused by the fact that he had been putting such fœtuses in bottles over many years.

DR. N. MCALISTER GREGG said that two things had been brought home to him at the meeting. First, when he saw the film "Science Against Cancer", he realized what a small part a humble clinician played. The second point was how little he knew about rubella. Dr. Gregg thanked the two speakers for their generous tribute to any part he might have played in the investigation. Dr. Gregg had been pleased to hear Professor Dods mention one aspect of the rubella question—that the matter did not rest with the diagnosis and with the disability suffered by the unfortunate child. Such a disaster had a very big influence on the home life. Dr. Gregg said that he had made many appeals for help for such badly afflicted people. Only the previous week he had had brought to him a child nine years old, with a mental age of anything less than twelve months. The child had been brought because the small amount of vision in one eye appeared to have gone. Examination of the child disclosed that the better eye was full of blood, and the left side of the face was extensively bruised. All through the interview the child stood thumping himself violently; if he was not doing that, he was trying to gouge his eyes out. Dr. Gregg felt strongly that such a child should not be allowed to stay in the family home; he should be removed. The second child in the family had had to stay in a boarding school, and very seldom returned home even for holidays. Children like the boy described should be cared for in an institution. Referring to Dr. Furber's remarks, that it was now possible to reassure parents that no further children would be affected by the rubella virus, Dr. Gregg told the story of two parents who took their first child's disability well, and acted on the advice that it would be worth while trying again. The result of the second pregnancy was the birth of healthy triplets, weighing respectively six, six, and five and a half pounds.

Dr. Donald Hunter spoke again, to comment on Dr. Gregg's statement that his contribution was that of a humble clinician by comparison with research workers in well-equipped laboratories. Dr. Hunter did not agree that clinicians should humble themselves, and insisted that Dr. Gregg was a great man whose name would live in the history of medical research because his work had established a new and fundamental principle. Dr. Hunter said that everything he had seen in Australia was remarkably English in character, and that by reason of his delightful powers of understatement Dr. Gregg was more English than the English.

Professor Dods, in reply, said that he was interested in Dr. Lancaster's comments about the epidemic of deaf-mutism amongst children born during the early months of 1899 and the extensive epidemic of measles and rubella during the latter half of 1898, which had apparently reached its peak approximately seven months before the majority of the affected children were born. That evidence, collected by Dr. Lancaster from the Commonwealth Statistician's reports and other medical records, helped to emphasize the unfortunate hiatus between statistical and clinical medicine and also suggested the possible value of the study of epidemicity of certain other congenital defects. Professor Dods was particularly glad that Dr. Donald Hunter had been present to challenge Dr. Gregg's natural humility and to emphasize the full significance of his outstanding discoveries.

Professor Mayes, in reply, said that he had a request to make. Firmly believing in the validity of Dr. Gregg's observations and deductions, he was collecting the embryos from pregnancies terminated because of rubella. Through Dr. Gregg, Professor Mayes had been privileged to meet Professor Ida Mann, who had played an important part from the embryological and ophthalmological points of view in the study of the conditions under discussion, and she had graciously consented to examine the specimens when he had a series that would be worth while. The series now consisted of about 15 or 16; he aimed at a series of 25 to

30 before embarking on the work. Therefore, in the interests of scientific assessment of the effect of rubella on the infant, he would appreciate the receipt from any practitioner of suitable embryos to add to the series.

Correspondence.

THE AUSTRALIAN TUBERCULOSIS ASSOCIATION.

SIR: At the British Medical Association congresses held in Adelaide in 1937 and in Perth in 1948, tuberculosis was the main subject under discussion, and on each occasion a resolution was passed at the plenary session pledging the support of the profession to measures designed for its more effective control in Australia.

In Perth the matter was carried a step further, and the first move was made towards the formation of an Australian Tuberculosis Association, the main object of which is to assist in every way possible in the control and prevention of tuberculosis. This association has been duly formed and incorporated, and a division has been established or is in process of formation in every State of the Commonwealth. Each State division has control of its own funds and has the fullest measure of autonomy, provided only that its policy does not clash with that of the parent body.

To function effectively the association and its divisions must have financial and other resources commensurate with the importance of the task they have undertaken. In view of the resolutions of congress it is confidently anticipated that members of the profession will play their part in assuring the success of this enterprise.

May we remind you of the words of the late Sir William Osler: "A last word on the subject of tuberculosis for the general practitioner. The leadership of the battle against this scourge is in your hands. Much has been done: much remains to do. By early diagnosis and prompt systematic treatment of individual cases, by the prompt recognition of contact cases, by striving in every possible way to improve the social condition of the poor, by joining actively in the work of local and national anti-tuberculosis societies you can help in the most important and the most hopeful campaign ever undertaken by the profession."

All members of the profession are urged to join and to take an active interest in their State division and to support the Christmas Seal Appeal being conducted by this association.

Tuberculosis is the last of the great infections of mankind still to be conquered. With a strong and united effort this can and will be done.

Yours, etc.,

H. S. NEWLAND, President.
D. R. W. COWAN, Honorary Secretary.

Australian Tuberculosis Association,
188 North Terrace,
Adelaide.

November 3, 1950.

ACUTE MYOCARDITIS.

SIR: I appreciate Dr. Saint's remarks and interest in the cases of acute myocarditis reported in the issue of your journal dated October 21, 1950, but regret that I cannot contribute any further pathological data that would help to solve the problem of the correct diagnosis in Case VI. The precise ætiology of that girl's illness was not determined—the myocarditis was the only positive feature of it remaining at autopsy.

Whilst agreeing that the illness of the girl summarized in Case VI possesses clinical features suggestive of *polyarteritis nodosa*, no evidence was discovered at autopsy to support this diagnosis. Particular attention was paid to the coronary arteries; they appeared normal to the naked eye, and no microscopic changes were seen in the vessels in a number of sections cut from two blocks of tissue of the heart wall. The renal vessels also appeared normal, and sections of the kidney studied microscopically did not show any evidence of arterial inflammation. The subpleural hæmorrhages were considered to be the usual petechiæ so often observed on the surface of the lung in sudden death.

Those who followed the autopsy on this girl were disappointed that it was not more revealing—only the girl's unexpected death was accounted for on the basis of myocarditis.

Yours, etc.,

KEITH BOWDEN.

City Morgue,
Melbourne,
November 8, 1950.

AN EFFICIENT RESUSCITATOR.

SIR: With the approach of the swimming season, the usual crop of drownings is to be expected.

It might be well to stress the inefficiency of the Schafer method of artificial respiration, the similar inefficiency of the Sylvester method, the much greater efficiency of the

FIGURE I.
The Kreiselman resuscitator. Right angle adapter for treatment of patient lying prone with head turned to one side.

rocking method of Eve, and to stimulate an inquiry into the rib traction method of Viswanathan, reported in *The Lancet* (1945), Volume I, page 238. This report indicates a greater efficiency than Eve's rocking method and requires no apparatus.

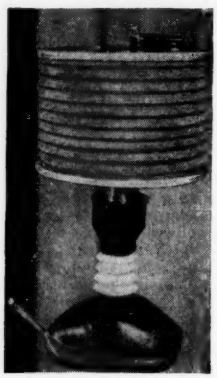

FIGURE II.
The Kreiselman resuscitator. Mask direct to resuscitator for treatment of patient lying on back.

Of the mechanical aids for artificial respiration, the simplest and most efficient is the Kreiselman resuscitator, of which two prints are enclosed (Figures I and II). This apparatus has been demonstrated in Melbourne. Similar demonstrations could be arranged in other centres.

It is earnestly hoped that this resuscitator may be manufactured in Australia. Some idea of the possible demand for it would stimulate the project.

Yours, etc.,

DOUGLAS G. RENTON, F.F.A.R.C.S.,
Anæsthetist, Neurosurgical Unit,
Alfred Hospital, Melbourne.

12 Collins Street,
Melbourne,
October 14, 1950.

Obituary.

EDWARD ALBERT WOODWARD.

DR. J. McF. ROSSELL has forwarded the following appreciation of the late Dr. Edward Albert Woodward.

After a brilliant scholastic and sporting record at the Sydney Church of England Grammar School, Dr. Ted Woodward went on to the university and fulfilled expectations there. He graduated with honours and represented in rowing and football. To many who knew him in those days it seemed that he should have applied his very real gifts to literature. This was what came easiest to him. But he made a success of his chosen profession. After return from active service in 1919, where he won the Military Cross, he practised at Emmaville and Grafton. It is in this latter district that his influence will be most felt. He was a man of very wide interests outside his work, in literature, sporting and the military field. He was one of those men who chose the better part, that is, general practice, instead of specializing.

For many years he had realized that his health was failing, and some two years ago he gave up general work and applied himself to pathology in Grafton. He bore these last few years of failing health with his usual cheerfulness and fortitude. Nothing pleased him more than to talk in his usual humorous strain of his younger days. To his wife and children, Dr. W. Woodward and Miss Barbara Woodward, goes the sympathy of the profession.

At the funeral service the following lines written by him in his last days were read. They explain his philosophy.

I too have dwelt in Arcady
And heard the Piper in the glade
And still a gay flute trills for me.

The piping shrilled and fell, and we
Danced in the sunlight, boy and maid:
I too have dwelt in Arcady.

So youth then swayed in ecstasy
To lilting tunes the piper played:
And still a gay flute trills for me.

The music falls to minor key:
I wait the last note undismayed.
I too have dwelt in Arcady.

The dance is done, and Time takes fee
Of Youth to write the flautist paid:
And still a gay flute trills for me.

The low sun through the olive tree
Makes of our green a chequered shade.
I too have dwelt in Arcady
And still a gay flute trills for me.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Annual Post-Graduate Oration, 1951.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that the fourth Post-Graduate Oration will be delivered in the Great Hall of the University of Sydney on the evening of Wednesday, April 4, 1951. The orator, Dr. K. S. Macarthur Brown, will speak on "Early Fleet Surgeons and the Establishment of the Sydney Hospital".

Those wishing to have their names placed on the invitation list are requested to communicate before February 1, 1951, with the Secretary, the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 5238, BW 7483.

Clinical Meeting at Balmoral Naval Hospital.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a clinical meeting will

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED NOVEMBER 4, 1950.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.[2]	Northern Territory.[2]	Australian Capital Territory.	Australia.[2]
Ankylostomiasis	*	..	..	..	2	..	..	..	2
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	1	1(1)	1	..	1	..	..	..	4
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	..	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	3	..	..	..	..	..	3
Diphtheria	12(7)	2	5(3)	..	2(2)	..	..	..	21
Dysentery (Amœbic)	*	..	..	..	1	..	..	..	1
Dysentery (Bacillary)	*	..	..	..	..	..	..	..	..
Encephalitis Lethargica	..	..	..	..	..	..	..	..	..
Erysipelas	*	*	*	1(1)	*	*	..	..	1
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	..	*	..	..	*	*	..	..
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	..	*	*	*	*	*	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	*	..	..	..	..	..	..	..	..
Measles	*	*	*	567(410)	*	*	..	..	567
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	19(10)	3	2	5(5)	..	*	..	..	29
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	2	1(1)	..	..	..	..	3
Rubella(*c*)	*	*	..	*	1	*	..	..	1
Scarlet Fever	24(11)	13(9)	35(31)	5(5)	6(3)	..	..	..	83
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	2	2(1)	*	*	*	*	*	4
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(*d*)	29(20)	14(7)	11(8)	9(5)	13(10)	..	..	1	77
Typhoid Fever(*e*)	1	..	..	..	..	..	..	..	1
Typhus (Endemic)(*f*)	1(1)	..	..	..	1(1)	..	..	..	2
Undulant Fever	..	2	..	..	..	..	..	..	2
Weil's Disease(*g*)	*	*	1	*	*	*	*	*	1
Whooping Cough	*	*	*	13(5)	*	*	..	..	13
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.

[2] Figures not available.

[3] Figures incomplete owing to absence of returns from the Northern Territory and Tasmania.

* Not notifiable.

(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

be held at the Balmoral Naval Hospital, Balmoral, on Tuesday, December 12, 1950, at 2 p.m., when Dr. Eric Susman will speak on "Epilepsy and Epileptic Variants". Clinical cases will be presented at 4 p.m., after afternoon tea. All members of the medical profession are invited to attend.

Naval, Military and Air Force.

APPOINTMENTS.

THE following appointments, promotions *et cetera* are promulgated in the *Commonwealth of Australia Gazette*, Number 66, of November 2, 1950.

ROYAL AUSTRALIAN AIR FORCE.

Citizen Air Force.

Air Force Reserve: Medical Branch.

The appointments of the following officers are terminated: (Temporary Squadron Leader) W. G. Gailey (262375), 17th July, 1950, Flight Lieutenant W. J. Stevenson (257483), 11th July, 1950.

The following former officers are appointed to commissions with the ranks indicated: (Temporary Squadron Leader) R. G. Skinner (021959), 11th March, 1950, (Flight Lieutenant) G. B. Goswell (267238), 25th July, 1950.

The following are appointed to a commission with the rank of Flight Lieutenant: Alexander Joseph May (277567), 7th July, 1950, Ian Archibald Waldie (257791), 21st August, 1950.

Medical Prizes.

THE AUSTRALIAN ORTHOPÆDIC ASSOCIATION PRIZE, 1952.

THE Australian Orthopædic Association will award its prize of twenty-five guineas for the best original and unpublished essay on "The Indications for, and End Results of, Excision of the Patella". Entrants for the prize are to be either sixth year medical students or graduates of not more than five years' standing at the date of closure. The essay shall not exceed 5000 words, and if no essay is deemed of sufficient merit the committee retains the right to withhold the prize. The publication rights of the essay shall belong to the Australian Orthopædic Association. Essays shall be typewritten with double spacing and should be in triplicate; they should be forwarded under a pseudonym to the Honorary Secretary, Dr. A. R. Hamilton, 135 Macquarie Street, Sydney. A separate sealed envelope should be enclosed, containing the name and address of the candidate, together with the pseudonym used. Entries will close on June 30, 1952.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Pearson, Donald Willis, M.B., 1950 (Univ. Sydney), 11 Alberta Street, Jannali.

Godby, Norman Russell, M.B., B.S., 1939 (Univ. Melbourne), Bodington Sanatorium, Wentworth Falls.

Burnett, Richard William, M.B., B.S., 1950 (Univ. Sydney), 8 San Juan, 6 Warners Avenue, Bondi.

Cohn, Siegfried, registered in accordance with the provisions of Section 17B of the *Medical Practitioners Act*, 1938-1945, 17 Keating Street, Maroubra.

Freilich, Herbert, M.B., B.S., 1947 (Univ. Sydney), 4 Arthur Street, Bellevue Hill.

Roper, John Ramsay, M.B., B.S., 1950 (Univ. Sydney), 66 Wallaroy Road, Woollahra.

Bartlett, Brian Harold, M.B., B.S., 1950 (Univ. Sydney), Sydney Hospital, Sydney.

The undermentioned has applied for election as a member of the South Australian Branch of the British Medical Association:

Storey, John Eric Macartney, M.B., B.S., 1942 (Univ. Sydney), 57 Woodville Road, Woodville.

Diary for the Month.

Nov. 28.—New South Wales Branch, B.M.A.: Ethics Committee.
Nov. 30.—New South Wales Branch, B.M.A.: Branch Meeting.
Nov. 30.—South Australian Branch, B.M.A.: Branch Meeting.
DEC. 5.—New South Wales Branch, B.M.A.: Executive and Finance Committee. Organization and Science Committee.
DEC. 6.—New South Wales Branch, B.M.A.: Special Groups Committee.
DEC. 6.—Victorian Branch, B.M.A.: Annual Meeting.
DEC. 6.—Western Australian Branch, B.M.A.: Council Meeting.
DEC. 7.—New South Wales Branch, B.M.A.: Clinical Meeting.
DEC. 7.—South Australian Branch, B.M.A.: Council Meeting.
DEC. 8.—Queensland Branch, B.M.A.: Annual Meeting.
DEC. 11.—Victorian Branch, B.M.A.: Executive Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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